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(54) Title: NOVEL G PROTEIN-COUPLED RECEPTORS

(57) Abstract: The present invention provides a gene encoding a G protein-coupled receptor termed nGPCR-x; constructs and recombinant host cells incorporating the genes; the nGPCR-x polypeptides encoded by the gene; antibodies to the nGPCR-x polypeptides; and methods of making and using all of the foregoing.

NOVEL G PROTEIN-COUPLED RECEPTORS

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application claims priority of Application Serial No. 60/187,828, filed March 8, 2000; Serial No. 60/187,715, filed March 8, 2000; Serial No. 60/187,929, filed March 8, 2000; Serial No. 60/187,930, filed March 8, 2000; Serial No. 60/187,825, filed March 8, 2000; Serial No. 60/187,833, filed March 8, 2000; Serial No. 60/187,830, filed March 8, 2000; Serial No. 60/187,829, filed March 8, 2000; Serial No. 60/187,582, filed March 8, 2000; Serial No. 60/187,581, filed March 8, 2000; Serial No. 60/187,714, filed March 8, 2000; Serial No. 60/189,294, filed March 8, 2000; Serial No. 60/187,874, filed March 8, 2000; Serial No. 60/187,928, filed March 8, 2000; Serial No. 60/188,049, filed March 8, 2000, each of which is hereby incorporated by reference in its entirety.

FIELD OF THE INVENTION

The present invention relates generally to the fields of genetics and cellular and molecular biology. More particularly, the invention relates to novel G protein coupled receptors, to polynucleotides that encode such novel receptors, to reagents such as antibodies, probes, primers and kits comprising such antibodies, probes, primers related to the same, and to methods which use the novel G protein coupled receptors, polynucleotides or reagents.

BACKGROUND OF THE INVENTION

The G protein-coupled receptors (GPCRs) form a vast superfamily of cell surface receptors which are characterized by an amino-terminal extracellular domain, a carboxyl-terminal intracellular domain, and a serpentine structure that passes through the cell membrane seven times. Hence, such receptors are sometimes also referred to as seven transmembrane (7TM) receptors. These seven transmembrane domains define three extracellular loops and three intracellular loops, in addition to the amino- and carboxy-terminal domains. The extracellular portions of the receptor have a role in recognizing

and binding one or more extracellular binding partners (*e.g.*, ligands), whereas the intracellular portions have a role in recognizing and communicating with downstream molecules in the signal transduction cascade.

The G protein-coupled receptors bind a variety of ligands including calcium ions, hormones, chemokines, neuropeptides, neurotransmitters, nucleotides, lipids, odorants, and even photons, and are important in the normal (and sometimes the aberrant) function of many cell types. [See generally Strosberg, *Eur. J. Biochem.* 196:1-10 (1991) and Bohm *et al., Biochem J.* 322:1-18 (1997).] When a specific ligand binds to its corresponding receptor, the ligand typically stimulates the receptor to activate a specific heterotrimeric guanine-nucleotide-binding regulatory protein (G-protein) that is coupled to the intracellular portion of the receptor. The G protein in turn transmits a signal to an effector molecule within the cell, by either stimulating or inhibiting the activity of that effector molecule. These effector molecules include adenylate cyclase, phospholipases and ion channels. Adenylate cyclase and phospholipases are enzymes that are involved in the production of the second messenger molecules cAMP, inositol triphosphate and diacyglycerol. It is through this sequence of events that an extracellular ligand stimuli exerts intracellular changes through a G protein-coupled receptor. Each such receptor has its own characteristic primary structure, expression pattern, ligand-binding profile, and intracellular effector system.

Because of the vital role of G protein-coupled receptors in the communication between cells and their environment, such receptors are attractive targets for therapeutic intervention, for example by activating or antagonizing such receptors. For receptors having a known ligand, the identification of agonists or antagonists may be sought specifically to enhance or inhibit the action of the ligand. Some G protein-coupled receptors have roles in disease pathogenesis (*e.g.*, certain chemokine receptors that act as HIV co-receptors may have a role in AIDS pathogenesis), and are attractive targets for therapeutic intervention even in the absence of knowledge of the natural ligand of the receptor. Other receptors are attractive targets for therapeutic intervention by virtue of their expression pattern in tissues or cell types that are themselves attractive targets for therapeutic intervention. Examples of this latter category of receptors include receptors expressed in immune cells, which can be targeted to either inhibit autoimmune responses

or to enhance immune responses to fight pathogens or cancer; and receptors expressed in the brain or other neural organs and tissues, which are likely targets in the treatment of mental disorder, depression, bipolar disease, or other neurological disorders. This latter category of receptor is also useful as a marker for identifying and/or purifying (*e.g.*, via fluorescence-activated cell sorting) cellular subtypes that express the receptor. Unfortunately, only a limited number of G protein receptors from the central nervous system (CNS) are known. Thus, a need exists for G protein-coupled receptors that have been identified and show promise as targets for therapeutic intervention in a variety of animals, including humans.

SUMMARY OF THE INVENTION

The present invention relates to an isolated nucleic acid molecule that comprises a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence homologous to sequences selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, or a fragment thereof. The nucleic acid molecule encodes at least a portion of nGPCR-x. In some embodiments, the nucleic acid molecule comprises a sequence that encodes a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, or a fragment thereof. In some embodiments, the nucleic acid molecule comprises a sequence homologous to a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, or a fragment thereof. In some embodiments, the nucleic acid molecule comprises a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, and fragments thereof.

According to some embodiments, the present invention provides vectors which comprise the nucleic acid molecule of the invention. In some embodiments, the vector is an expression vector.

According to some embodiments, the present invention provides host cells which comprise the vectors of the invention. In some embodiments, the host cells comprise expression vectors.

The present invention provides an isolated nucleic acid molecule comprising a nucleotide sequence complementary to at least a portion of a sequence selected from the

group consisting of SEQ ID NO:1 to SEQ ID NO:134, said portion comprising at least 10 nucleotides.

The present invention provides a method of producing a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, or a homolog or fragment thereof. The method comprising the steps of introducing a recombinant expression vector that includes a nucleotide sequence that encodes the polypeptide into a compatible host cell, growing the host cell under conditions for expression of the polypeptide and recovering the polypeptide.

The present invention provides an isolated antibody which binds to an epitope on a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, or a homolog or fragment thereof.

The present invention provides an method of inducing an immune response in a mammal against a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, or a homolog or fragment thereof. The method comprises administering to a mammal an amount of the polypeptide sufficient to induce said immune response.

The present invention provides a method for identifying a compound which binds nGPCR-x. The method comprises the steps of contacting nGPCR-x with a compound and determining whether the compound binds nGPCR-x.

The present invention provides a method for identifying a compound which binds a nucleic acid molecule encoding nGPCR-x. The method comprises the steps of contacting said nucleic acid molecule encoding nGPCR-x with a compound and determining whether said compound binds said nucleic acid molecule.

The present invention provides a method for identifying a compound which modulates the activity of nGPCR-x. The method comprises the steps of contacting nGPCR-x with a compound and determining whether nGPCR-x activity has been modulated.

The present invention provides a method of identifying an animal homolog of nGPCR-x. The method comprises the steps screening a nucleic acid database of the animal with a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, or a portion thereof and determining whether a portion of said library or database

is homologous to said sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, or portion thereof.

The present invention provides a method of identifying an animal homolog of nGPCR-x. The methods comprises the steps screening a nucleic acid library of the animal with a nucleic acid molecule having a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, or a portion thereof; and determining whether a portion of said library or database is homologous to said sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, or a portion thereof.

Another aspect of the present invention relates to methods of screening a human subject to diagnose a disorder affecting the brain or genetic predisposition therefor. The methods comprise the steps of assaying nucleic acid of a human subject to determine a presence or an absence of a mutation altering an amino acid sequence, expression, or biological activity of at least one nGPCR-x that is expressed in the brain. The nGPCR-x comprise an amino acid sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, and allelic variants thereof. A diagnosis of the disorder or predisposition is made from the presence or absence of the mutation. The presence of a mutation altering the amino acid sequence, expression, or biological activity of the nGPCR-x in the nucleic acid correlates with an increased risk of developing the disorder.

The present invention further relates to methods of screening for a nGPCR-x hereditary mental disorder genotype in a human patient. The methods comprise the steps of providing a biological sample comprising nucleic acid from the patient, in which the nucleic acid includes sequences corresponding to alleles of nGPCR-x. The presence of one or more mutations in the nGPCR-x allele is indicative of a hereditary mental disorder genotype.

The present invention provides kits for screening a human subject to diagnose mental disorder or a genetic predisposition therefor. The kits include an oligonucleotide useful as a probe for identifying polymorphisms in a human nGPCR-x gene. The oligonucleotide comprises 6-50 nucleotides in a sequence that is identical or complementary to a sequence of a wild type human nGPCR-x gene sequence or nGPCR-x coding sequence, except for one sequence difference selected from the group consisting of a nucleotide addition, a nucleotide deletion, or nucleotide substitution. The kit also

includes a media packaged with the oligonucleotide. The media contains information for identifying polymorphisms that correlate with mental disorder or a genetic predisposition therefor, the polymorphisms being identifiable using the oligonucleotide as a probe.

The present invention further relates to methods of identifying nGPCR-x allelic variants that correlates with mental disorders. The methods comprise the steps of providing biological samples that comprise nucleic acid from a human patient diagnosed with a mental disorder, or from the patient's genetic progenitors or progeny, and detecting in the nucleic acid the presence of one or more mutations in an nGPCR-x that is expressed in the brain. The nGPCR-x comprises an amino acid sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, and allelic variants thereof. The nucleic acid includes sequences corresponding to the gene or genes encoding nGPCR-x. The one or more mutations detected indicate an allelic variant that correlates with a mental disorder.

The present invention further relates to purified polynucleotides comprising nucleotide sequences encoding alleles of nGPCR-x from a human with mental disorder. The polynucleotide hybridizes to the complement of a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134 under the following hybridization conditions: (a) hybridization for 16 hours at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaC1, 10% dextran sulfate and (b) washing 2 times for 30 minutes at 60°C in a wash solution comprising 0.1x SSC and 1% SDS. The polynucleotide that encodes nGPCR-x amino acid sequence of the human differs from a sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268 by at least one residue.

The present invention also provides methods for identifying a modulator of biological activity of nGPCR-x comprising the steps of contacting a cell that expresses nGPCR-x in the presence and in the absence of a putative modulator compound and measuring nGPCR-x biological activity in the cell. The decreased or increased nGPCR-x biological activity in the presence versus absence of the putative modulator is indicative of a modulator of biological activity.

The present invention further provides methods to identify compounds useful for the treatment of mental disorders. The methods comprise the steps of contacting a

composition comprising nGPCR-x with a compound suspected of binding nGPCR-x. The binding between nGPCR-x and the compound suspected of binding nGPCR-x is detected. Compounds identified as binding nGPCR-x are candidate compounds useful for the treatment of mental disorder. Compounds identified as binding nGPCR-x may be further tested in other assays including, but not limited to, *in vivo* models, in order to confirm or quantitate their activity.

The present invention further provides methods for identifying a compound useful as a modulator of binding between nGPCR-x and a binding partner of nGPCR-x. The methods comprise the steps of contacting the binding partner and a composition comprising nGPCR-x in the presence and in the absence of a putative modulator compound and detecting binding between the binding partner and nGPCR-x. Decreased or increased binding between the binding partner and nGPCR-x in the presence of the putative modulator, as compared to binding in the absence of the putative modulator is indicative a modulator compound useful for the treatment of a related disease or disorder. Compounds identified as modulating binding between nGPCR-x and a nGPCR-x binding partner may be further tested in other assays including, but not limited to, *in vivo* models, in order to confirm or quantitate their activity as modulators.

Another aspect of the present invention relates to methods of purifying a G protein from a sample containing a G protein. The methods comprise the steps of contacting the sample with an nGPCR-x for a time sufficient to allow the G protein to form a complex with the nGPCR-x; isolating the complex from remaining components of the sample; maintaining the complex under conditions which result in dissociation of the G protein from the nGPCR-x; and isolating said G protein from the nGPCR-x.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Definitions

Various definitions are made throughout this document. Most words have the meaning that would be attributed to those words by one skilled in the art. Words specifically defined either below or elsewhere in this document have the meaning provided in the context of the present invention as a whole and as are typically understood by those skilled in the art.

"Synthesized" as used herein and understood in the art, refers to polynucleotides produced by purely chemical, as opposed to enzymatic, methods. "Wholly" synthesized DNA sequences are therefore produced entirely by chemical means, and "partially" synthesized DNAs embrace those wherein only portions of the resulting DNA were produced by chemical means.

By the term "region" is meant a physically contiguous portion of the primary structure of a biomolecule. In the case of proteins, a region is defined by a contiguous portion of the amino acid sequence of that protein.

The term "domain" is herein defined as referring to a structural part of a biomolecule that contributes to a known or suspected function of the biomolecule. Domains may be co-extensive with regions or portions thereof; domains may also incorporate a portion of a biomolecule that is distinct from a particular region, in addition to all or part of that region . Examples of GPCR protein domains include, but are not limited to, the extracellular (*i.e.*, N-terminal), transmembrane and cytoplasmic (*i.e.*, C-terminal) domains, which are co-extensive with like-named regions of GPCRs; each of the seven transmembrane segments of a GPCR; and each of the loop segments (both extracellular and intracellular loops) connecting adjacent transmembrane segments.

As used herein, the term "activity" refers to a variety of measurable indicia suggesting or revealing binding, either direct or indirect; affecting a response, i.e. having a measurable affect in response to some exposure or stimulus, including, for example, the affinity of a compound for directly binding a polypeptide or polynucleotide of the invention, or, for example, measurement of amounts of upstream or downstream proteins or other similar functions after some stimulus or event.

Unless indicated otherwise, as used herein, the abbreviation in lower case (gpcr) refers to a gene, cDNA, RNA or nucleic acid sequence, while the upper case version (GPCR) refers to a protein, polypeptide, peptide, oligopeptide, or amino acid sequence. The term "nGPCR-x" refers to any of the nGPCRs taught herein, while specific reference to a nGPCR (for example nGPCR-2073) refers only to that specific nGPCR.

As used herein, the term "antibody" is meant to refer to complete, intact antibodies, and Fab, Fab', F(ab)2, and other fragments thereof. Complete, intact

antibodies include monoclonal antibodies such as murine monoclonal antibodies, chimeric antibodies and humanized antibodies.

As used herein, the term "binding" means the physical or chemical interaction between two proteins or compounds or associated proteins or compounds or combinations thereof. Binding includes ionic, non-ionic, Hydrogen bonds, Van der Waals, hydrophobic interactions, etc. The physical interaction, the binding, can be either direct or indirect, indirect being through or due to the effects of another protein or compound. Direct binding refers to interactions that do not take place through or due to the effect of another protein or compound but instead are without other substantial chemical intermediates. Binding may be detected in many different manners. As a non-limiting example, the physical binding interaction between a nGPCR-x of the invention and a compound can be detected using a labeled compound. Alternatively, functional evidence of binding can be detected using, for example, a cell transfected with and expressing a nGPCR-x of the invention. Binding of the transfected cell to a ligand of the nGPCR-x that was transfected into the cell provides functional evidence of binding. Other methods of detecting binding are well known to those of skill in the art.

As used herein, the term "compound" means any identifiable chemical or molecule, including, but not limited to, small molecule, peptide, protein, sugar, nucleotide, or nucleic acid, and such compound can be natural or synthetic.

As used herein, the term "complementary" refers to Watson-Crick basepairing between nucleotide units of a nucleic acid molecule.

As used herein, the term "contacting" means bringing together, either directly or indirectly, a compound into physical proximity to a polypeptide or polynucleotide of the invention. The polypeptide or polynucleotide can be in any number of buffers, salts, solutions *etc.* Contacting includes, for example, placing the compound into a beaker, microtiter plate, cell culture flask, or a microarray, such as a gene chip, or the like, which contains the nucleic acid molecule, or polypeptide encoding the nGPCR or fragment thereof.

As used herein, the phrase "homologous nucleotide sequence," or "homologous amino acid sequence," or variations thereof, refers to sequences characterized by a homology, at the nucleotide level or amino acid level, of at least the specified percentage.

Homologous nucleotide sequences include those sequences coding for isoforms of proteins. Such isoforms can be expressed in different tissues of the same organism as a result of, for example, alternative splicing of RNA. Alternatively, isoforms can be encoded by different genes. Homologous nucleotide sequences include nucleotide sequences encoding for a protein of a species other than humans, including, but not limited to, mammals. Homologous nucleotide sequences also include, but are not limited to, naturally occurring allelic variations and mutations of the nucleotide sequences set forth herein. A homologous nucleotide sequence does not, however, include the nucleotide sequence encoding other known GPCRs. Homologous amino acid sequences include those amino acid sequences which contain conservative amino acid substitutions and which polypeptides have the same binding and/or activity. A homologous amino acid sequence does not, however, include the amino acid sequence encoding other known GPCRs. Percent homology can be determined by, for example, the Gap program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, Madison WI), using the default settings, which uses the algorithm of Smith and Waterman (Adv. Appl. Math., 1981, 2, 482-489, which is incorporated herein by reference in its entirety).

As used herein, the term "isolated" nucleic acid molecule refers to a nucleic acid molecule (DNA or RNA) that has been removed from its native environment. Examples of isolated nucleic acid molecules include, but are not limited to, recombinant DNA molecules contained in a vector, recombinant DNA molecules maintained in a heterologous host cell, partially or substantially purified nucleic acid molecules, and synthetic DNA or RNA molecules.

As used herein, the terms “modulates” or “modifies” means an increase or decrease in the amount, quality, or effect of a particular activity or protein.

As used herein, the term “oligonucleotide” refers to a series of linked nucleotide residues which has a sufficient number of bases to be used in a polymerase chain reaction (PCR). This short sequence is based on (or designed from) a genomic or cDNA sequence and is used to amplify, confirm, or reveal the presence of an identical, similar or complementary DNA or RNA in a particular cell or tissue. Oligonucleotides comprise portions of a DNA sequence having at least about 10 nucleotides and as many as about 50

nucleotides, preferably about 15 to 30 nucleotides. They are chemically synthesized and may be used as probes.

As used herein, the term "probe" refers to nucleic acid sequences of variable length, preferably between at least about 10 and as many as about 6,000 nucleotides, depending on use. They are used in the detection of identical, similar, or complementary nucleic acid sequences. Longer length probes are usually obtained from a natural or recombinant source, are highly specific and much slower to hybridize than oligomers. They may be single- or double-stranded and carefully designed to have specificity in PCR, hybridization membrane-based, or ELISA-like technologies.

The term "preventing" refers to decreasing the probability that an organism contracts or develops an abnormal condition.

The term "treating" refers to having a therapeutic effect and at least partially alleviating or abrogating an abnormal condition in the organism.

The term "therapeutic effect" refers to the inhibition or activation factors causing or contributing to the abnormal condition. A therapeutic effect relieves to some extent one or more of the symptoms of the abnormal condition. In reference to the treatment of abnormal conditions, a therapeutic effect can refer to one or more of the following: (a) an increase in the proliferation, growth, and/or differentiation of cells; (b) inhibition (*i.e.*, slowing or stopping) of cell death; (c) inhibition of degeneration; (d) relieving to some extent one or more of the symptoms associated with the abnormal condition; and (e) enhancing the function of the affected population of cells. Compounds demonstrating efficacy against abnormal conditions can be identified as described herein.

The term "abnormal condition" refers to a function in the cells or tissues of an organism that deviates from their normal functions in that organism. An abnormal condition can relate to cell proliferation, cell differentiation, cell signaling, or cell survival. An abnormal condition may also include obesity, diabetic complications such as retinal degeneration, and irregularities in glucose uptake and metabolism, and fatty acid uptake and metabolism.

Abnormal cell proliferative conditions include cancers such as fibrotic and mesangial disorders, abnormal angiogenesis and vasculogenesis, wound healing, psoriasis, diabetes mellitus, and inflammation.

Abnormal differentiation conditions include, but are not limited to, neurodegenerative disorders, slow wound healing rates, and slow tissue grafting healing rates. Abnormal cell signaling conditions include, but are not limited to, psychiatric disorders involving excess neurotransmitter activity.

Abnormal cell survival conditions may also relate to conditions in which programmed cell death (apoptosis) pathways are activated or abrogated. A number of protein kinases are associated with the apoptosis pathways. Aberrations in the function of any one of the protein kinases could lead to cell immortality or premature cell death.

The term "administering" relates to a method of incorporating a compound into cells or tissues of an organism. The abnormal condition can be prevented or treated when the cells or tissues of the organism exist within the organism or outside of the organism. Cells existing outside the organism can be maintained or grown in cell culture dishes. For cells harbored within the organism, many techniques exist in the art to administer compounds, including (but not limited to) oral, parenteral, dermal, injection, and aerosol applications. For cells outside of the organism, multiple techniques exist in the art to administer the compounds, including (but not limited to) cell microinjection techniques, transformation techniques and carrier techniques.

The abnormal condition can also be prevented or treated by administering a compound to a group of cells having an aberration in a signal transduction pathway to an organism. The effect of administering a compound on organism function can then be monitored. The organism is preferably a mouse, rat, rabbit, guinea pig or goat, more preferably a monkey or ape, and most preferably a human.

By "amplification" it is meant increased numbers of DNA or RNA in a cell compared with normal cells. "Amplification" as it refers to RNA can be the detectable presence of RNA in cells, since in some normal cells there is no basal expression of RNA. In other normal cells, a basal level of expression exists, therefore in these cases amplification is the detection of at least 1 to 2-fold, and preferably more, compared to the basal level.

As used herein, the phrase "stringent hybridization conditions" or "stringent conditions" refers to conditions under which a probe, primer, or oligonucleotide will hybridize to its target sequence, but to no other sequences. Stringent conditions are

sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures. Generally, stringent conditions are selected to be about 5°C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength and pH. The T_m is the temperature (under defined ionic strength, pH and nucleic acid concentration) at which 50% of the probes complementary to the target sequence hybridize to the target sequence at equilibrium. Since the target sequences are generally present in excess, at T_m, 50% of the probes are occupied at equilibrium. Typically, stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion (or other salts)at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes, primers or oligonucleotides (e.g. 10 to 50 nucleotides) and at least about 60°C for longer probes, primers or oligonucleotides. Stringent conditions may also be achieved with the addition of destabilizing agents, such as formamide.

The amino acid sequences are presented in the amino to carboxy direction, from left to right. The amino and carboxy groups are not presented in the sequence. The nucleotide sequences are presented by single strand only, in the 5' to 3' direction, from left to right. Nucleotides and amino acids are represented in the manner recommended by the IUPAC-IUB Biochemical Nomenclature Commission or (for amino acids) by three letters code.

Polynucleotides

The present invention provides purified and isolated polynucleotides (*e.g.*, DNA sequences and RNA transcripts, both sense and complementary antisense strands, both single- and double-stranded, including splice variants thereof) that encode unknown G protein-coupled receptors heretofore termed novel GPCRs, or nGPCRs. These genes are described herein and designated herein collectively as nGPCR-x (where x is 2356, 2357, 2358, 2359, 2360, 2361, 2362, 2363, 2364, 2365, 2366, 2367, 2368, 2369, 2370, 2371, 2372, 2373, 2374, 2375, 2376, 2377, 2378, 2379, 2380, 2381, 2382, 2383, 2384, 2385, 2386, 2387, 2388, 2389, 2390, 2391, 2392, 2393, 2394, 2395, 2396, 2397, 2398, 2399, 2400, 2401, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 2337, 2338, 2339, 2340, 2341, 2342, 2343, 2344, 2345, 2402, 2403, 2404, 2405, 2406, 2407, 2408, 2409, 2410, 2411, 2412, 2413, 2414, 2415, 2416, 2417, 2418, 2419, 2420, 2421, 2422, 2423, 2424, 2425, 2426,

2427, 2428, 2429, 2430, 2431, 2432, 2433, 2434, 2435, 2436, 2437, 2438, 2439, 2440, 2441, 2442, 2443, 2444, 2445, 2446, 2447, 2448, 2449, 2450, 2451, 2452, 2453, 2454, 2455, 2456, 2457, 2458, 2459, 2460, 2461, 2462, 2463, 2464, 2465, 2466, 2467, 2468, and 74). Table 1 below identifies the novel gene sequence nGPCR-x designation, the SEQ ID NO: of the gene sequence, the SEQ ID NO: of the polypeptide encoded thereby, and the U.S. Provisional Application in which the gene sequence has been disclosed.

Table 1

nGPCR	Nucleotide Sequence (SEQ ID NO:)	Amino acid Sequence (SEQ ID NO:)	Originally filed in:		nGCPR	Nucleotide Sequence (SEQ ID NO:)	Amino acid Sequence (SEQ ID NO:)	Originally filed in:
2356	1	135	A		2403	68	202	H
2357	2	136	A		2404	69	203	H
2358	3	137	A		2405	70	204	H
2359	4	138	A		2406	71	205	H
2360	5	139	A		2407	72	206	H
2361	6	140	A		2408	73	207	H
2362	7	141	A		2409	74	208	H
2363	8	142	A		2410	75	209	H
2364	9	143	A		2411	76	210	H
2365	10	144	A		2412	77	211	I
2366	11	145	B		2413	78	212	I
2367	12	146	B		2414	79	213	I
2368	13	147	B		2415	80	214	I
2369	14	148	B		2416	81	215	I
2370	15	149	B		2417	82	216	I
2371	16	150	B		2418	83	217	I
2372	17	151	B		2419	84	218	I
2373	18	142	B		2420	85	219	I
2374	19	153	B		2421	86	220	I
2375	20	154	B		2422	87	221	J
2376	21	155	C		2423	88	222	J
2377	22	156	C		2424	89	223	J
2378	23	157	C		2425	90	224	J
2379	24	158	C		2426	91	225	J
2380	25	159	C		2427	92	226	J
2381	26	160	C		2428	93	227	J
2382	27	161	C		2429	94	228	J
2383	28	162	C		2430	95	229	J
2384	29	163	C		2431	96	230	J
2385	30	164	C		2432	97	231	K
2386	31	165	D		2433	98	232	K
2387	32	166	D		2434	99	233	K
2388	33	167	D		2435	100	234	K
2389	34	168	D		2436	101	235	K
2390	35	169	D		2437	102	236	K
2391	36	170	D		2438	103	237	K
2392	37	171	D		2439	104	238	K
2393	38	172	D		2440	105	239	K
2394	39	173	D		2441	106	240	K
2395	40	174	D		2442	107	241	L
2396	41	175	E		2443	108	242	L

2397	42	176	E		2444	109	243	L
2398	43	177	E		2445	110	244	L
2399	44	178	E		2446	111	245	L
2400	45	179	E		2447	112	246	L
2401	46	180	E		2448	113	247	L
75	47	181	F		2449	114	248	L
76	48	182	F		2450	115	249	L
77	49	183	F		2451	116	250	L
78	50	184	F		2451	117	251	M
79	51	185	F		2453	118	252	M
80	52	186	F		2454	119	253	M
81	53	187	F		2455	120	254	M
82	54	188	F		2456	121	255	M
83	55	189	F		2457	122	256	M
84	56	190	F		2458	123	257	M
85	57	191	G		2459	124	258	M
2337	58	192	G		2460	125	259	M
2338	59	193	G		2461	126	260	M
2339	60	194	G		3462	127	261	N
2340	61	195	G		2463	128	262	N
2341	62	196	G		2464	129	263	N
2342	63	197	G		2465	130	264	N
2343	64	198	G		2466	131	265	N
2344	65	199	G		2467	132	266	N
2345	66	200	G		2568	133	267	N
2402	67	201	H		74	134	268	O

Legend

A= Ser. No. 60/187,828
B= Ser. No. 60/187,715
C= Ser. No. 60/187,929
D= Ser. No. 60/187,930
E= Ser. No. 60/187,825
F= Ser. No. 60/187,833
G= Ser. No. 60/187,830
H= Ser. No. 60/187,829
I= Ser. No. 60/187,582
J= Ser. No. 60/187,581
K= Ser. No. 60/187,714
L= Ser. No. 60/189,294
M= Ser. No. 60/187,874
N= Ser. No. 60/187,928
O= Ser. No. 60/188,049

When a specific nGPCR is identified (for example nGPCR-2344), it is understood that only that specific nGPCR is being referred to.

As described in Example 5 below, the gene encoding nGPCR-74 (nucleic acid sequence SEQ ID NO:134, amino acid sequence SEQ ID NO:268) has been detected in brain tissue indicating that this nGPCR protein is a neuroreceptor. It is well known that other nGPCR-x are expressed in many different tissues, including the brain. Accordingly, the nGPCR-x of the present invention may be useful, *inter alia*, fortreating and/or diagnosing mental disorders. Following the techniques described in Example 5, below, those skilled in the art could readily ascertain if nGPCR-x is expressed in a particular tissue or region.

The invention provides purified and isolated polynucleotides (*e.g.*, cDNA, genomic DNA, synthetic DNA, RNA, or combinations thereof, whether single- or double-stranded) that comprise a nucleotide sequence encoding the amino acid sequence of the polypeptides of the invention. Such polynucleotides are useful for recombinantly expressing the receptor and also for detecting expression of the receptor in cells (*e.g.*, using Northern hybridization and *in situ* hybridization assays). Such polynucleotides also are useful in the design of antisense and other molecules for the suppression of the expression of nGPCR-x in a cultured cell, a tissue, or an animal; for therapeutic purposes; or to provide a model for diseases or conditions characterized by aberrant nGPCR-x expression. Specifically excluded from the definition of polynucleotides of the invention are entire isolated, non-recombinant native chromosomes of host cells. A preferred polynucleotide has a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, which correspond to naturally occurring nGPCR-x sequences. It will be appreciated that numerous other polynucleotide sequences exist that also encode nGPCR-x having the sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, due to the well-known degeneracy of the universal genetic code.

The invention also provides a purified and isolated polynucleotide comprising a nucleotide sequence that encodes a mammalian polypeptide, wherein the polynucleotide hybridizes to a polynucleotide having the sequence set forth in sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, or the non-coding strand complementary thereto, under the following hybridization conditions:

(a) hybridization for 16 hours at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaCl, 10% dextran sulfate; and

(b) washing 2 times for 30 minutes each at 60°C in a wash solution comprising 0.1% SSC, 1% SDS. Polynucleotides that encode a human allelic variant are highly preferred.

The present invention relates to molecules which comprise the gene sequences that encode the nGPCRs; constructs and recombinant host cells incorporating the gene sequences; the novel GPCR polypeptides encoded by the gene sequences; antibodies to the polypeptides and homologs; kits employing the polynucleotides and polypeptides, and methods of making and using all of the foregoing. In addition, the present invention

relates to homologs of the gene sequences and of the polypeptides and methods of making and using the same.

Genomic DNA of the invention comprises the protein-coding region for a polypeptide of the invention and is also intended to include allelic variants thereof. It is widely understood that, for many genes, genomic DNA is transcribed into RNA transcripts that undergo one or more splicing events wherein intron (*i.e.*, non-coding regions) of the transcripts are removed, or "spliced out." RNA transcripts that can be spliced by alternative mechanisms, and therefore be subject to removal of different RNA sequences but still encode a nGPCR-x polypeptide, are referred to in the art as splice variants which are embraced by the invention. Splice variants comprehended by the invention therefore are encoded by the same original genomic DNA sequences but arise from distinct mRNA transcripts. Allelic variants are modified forms of a wild-type gene sequence, the modification resulting from recombination during chromosomal segregation or exposure to conditions which give rise to genetic mutation. Allelic variants, like wild type genes, are naturally occurring sequences (as opposed to non-naturally occurring variants that arise from *in vitro* manipulation).

The invention also comprehends cDNA that is obtained through reverse transcription of an RNA polynucleotide encoding nGPCR-x (conventionally followed by second strand synthesis of a complementary strand to provide a double-stranded DNA).

Preferred DNA sequences encoding human nGPCR-x polypeptides are selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134. A preferred DNA of the invention comprises a double stranded molecule along with the complementary molecule (the "non-coding strand" or "complement") having a sequence unambiguously deducible from the coding strand according to Watson-Crick base-pairing rules for DNA. Also preferred are other polynucleotides encoding the nGPCR-x polypeptide selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, which differ in sequence from the polynucleotides selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, by virtue of the well-known degeneracy of the universal nuclear genetic code.

The invention further embraces other species, preferably mammalian, homologs of the human nGPCR-x DNA. Species homologs, sometimes referred to as "orthologs," in general, share at least 35%, at least 40%, at least 45%, at least 50%, at least 60%, at least

65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% homology with human DNA of the invention. Generally, percent sequence "homology" with respect to polynucleotides of the invention may be calculated as the percentage of nucleotide bases in the candidate sequence that are identical to nucleotides in the nGPCR-x sequence set forth in sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity.

Polynucleotides of the invention permit identification and isolation of polynucleotides encoding related nGPCR-x polypeptides, such as human allelic variants and species homologs, by well-known techniques including Southern and/or Northern hybridization, and polymerase chain reaction (PCR). Examples of related polynucleotides include human and non-human genomic sequences, including allelic variants, as well as polynucleotides encoding polypeptides homologous to nGPCR-x and structurally related polypeptides sharing one or more biological, immunological, and/or physical properties of nGPCR-x. Non-human species genes encoding proteins homologous to nGPCR-x can also be identified by Southern and/or PCR analysis and are useful in animal models for nGPCR-x disorders. Knowledge of the sequence of a human nGPCR-x DNA also makes possible through use of Southern hybridization or polymerase chain reaction (PCR) the identification of genomic DNA sequences encoding nGPCR-x expression control regulatory sequences such as promoters, operators, enhancers, repressors, and the like. Polynucleotides of the invention are also useful in hybridization assays to detect the capacity of cells to express nGPCR-x. Polynucleotides of the invention may also provide a basis for diagnostic methods useful for identifying a genetic alteration(s) in a nGPCR-x locus that underlies a disease state or states, which information is useful both for diagnosis and for selection of therapeutic strategies.

According to the present invention, the nGPCR-x nucleotide sequences disclosed herein may be used to identify homologs of the nGPCR-x, in other animals, including but not limited to humans and other mammals, and invertebrates. Any of the nucleotide sequences disclosed herein, or any portion thereof, can be used, for example, as probes to screen databases or nucleic acid libraries, such as, for example, genomic or cDNA libraries, to identify homologs, using screening procedures well known to those skilled in

the art. Accordingly, homologs having at least 50%, more preferably at least 60%, more preferably at least 70%, more preferably at least 80%, more preferably at least 90%, more preferably at least 95%, and most preferably at least 100% homology with nGPCR-x sequences can be identified.

The disclosure herein of full-length polynucleotides encoding nGPCR-x polypeptides makes readily available to the worker of ordinary skill in the art every possible fragment of the full-length polynucleotide.

One preferred embodiment of the present invention provides an isolated nucleic acid molecule comprising a sequence homologous sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, and fragments thereof. Another preferred embodiment provides an isolated nucleic acid molecule comprising a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, and fragments thereof.

As used in the present invention, fragments of nGPCR-x-encoding polynucleotides comprise at least 10, and preferably at least 12, 14, 16, 18, 20, 25, 50, or 75 consecutive nucleotides of a polynucleotide encoding nGPCR-x. Preferably, fragment polynucleotides of the invention comprise sequences unique to the nGPCR-x-encoding polynucleotide sequence, and therefore hybridize under highly stringent or moderately stringent conditions only (*i.e.*, "specifically") to polynucleotides encoding nGPCR-x (or fragments thereof). Polynucleotide fragments of genomic sequences of the invention comprise not only sequences unique to the coding region, but also include fragments of the full-length sequence derived from introns, regulatory regions, and/or other non-translated sequences. Sequences unique to polynucleotides of the invention are recognizable through sequence comparison to other known polynucleotides, and can be identified through use of alignment programs routinely utilized in the art, *e.g.*, those made available in public sequence databases. Such sequences also are recognizable from Southern hybridization analyses to determine the number of fragments of genomic DNA to which a polynucleotide will hybridize. Polynucleotides of the invention can be labeled in a manner that permits their detection, including radioactive, fluorescent, and enzymatic labeling.

Fragment polynucleotides are particularly useful as probes for detection of full-length or fragments of nGPCR-x polynucleotides. One or more polynucleotides can be

included in kits that are used to detect the presence of a polynucleotide encoding nGPCR-x, or used to detect variations in a polynucleotide sequence encoding nGPCR-x.

The invention also embraces DNAs encoding nGPCR-x polypeptides that hybridize under moderately stringent or high stringency conditions to the non-coding strand, or complement, of the polynucleotides set forth in sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134.

Exemplary highly stringent hybridization conditions are as follows: hybridization at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaCl, 10% Dextran sulfate, and washing twice for 30 minutes at 60°C in a wash solution comprising 0.1X SSC and 1% SDS. It is understood in the art that conditions of equivalent stringency can be achieved through variation of temperature and buffer, or salt concentration as described Ausubel *et al.* (Eds.), Protocols in Molecular Biology, John Wiley & Sons (1994), pp. 6.0.3 to 6.4.10. Modifications in hybridization conditions can be empirically determined or precisely calculated based on the length and the percentage of guanosine/cytosine (GC) base pairing of the probe. The hybridization conditions can be calculated as described in Sambrook, *et al.*, (Eds.), Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press: Cold Spring Harbor, New York (1989), pp. 9.47 to 9.51.

With the knowledge of the nucleotide sequence information disclosed in the present invention, one skilled in the art can identify and obtain nucleotide sequences which encode nGPCR-x from different sources (*i.e.*, different tissues or different organisms) through a variety of means well known to the skilled artisan and as disclosed by, for example, Sambrook et al., "Molecular cloning: a laboratory manual", Second Edition, Cold Spring Harbor Press, Cold Spring Harbor, NY (1989), which is incorporated herein by reference in its entirety.

For example, DNA that encodes nGPCR-x may be obtained by screening of mRNA, cDNA, or genomic DNA with oligonucleotide probes generated from the nGPCR-x gene sequence information provided herein. Probes may be labeled with a detectable group, such as a fluorescent group, a radioactive atom or a chemiluminescent group in accordance with procedures known to the skilled artisan and used in conventional hybridization assays, as described by, for example, Sambrook *et al.*

A nucleic acid molecule comprising any of the nGPCR-x nucleotide sequences described above can alternatively be synthesized by use of the polymerase chain reaction (PCR) procedure, with the PCR oligonucleotide primers produced from the nucleotide sequences provided herein. See U.S. Patent Numbers 4,683,195 to Mullis *et al.* and 4,683,202 to Mullis. The PCR reaction provides a method for selectively increasing the concentration of a particular nucleic acid sequence even when that sequence has not been previously purified and is present only in a single copy in a particular sample. The method can be used to amplify either single- or double-stranded DNA. The essence of the method involves the use of two oligonucleotide probes to serve as primers for the template-dependent, polymerase mediated replication of a desired nucleic acid molecule.

A wide variety of alternative cloning and *in vitro* amplification methodologies are well known to those skilled in the art. Examples of these techniques are found in, for example, Berger *et al.*, *Guide to Molecular Cloning Techniques*, Methods in Enzymology 152, Academic Press, Inc., San Diego, CA (Berger), which is incorporated herein by reference in its entirety.

Automated sequencing methods can be used to obtain or verify the nucleotide sequence of nGPCR-x. The nGPCR-x nucleotide sequences of the present invention are believed to be 100% accurate. However, as is known in the art, nucleotide sequence obtained by automated methods may contain some errors. Nucleotide sequences determined by automation are typically at least about 90%, more typically at least about 95% to at least about 99.9% identical to the actual nucleotide sequence of a given nucleic acid molecule. The actual sequence may be more precisely determined using manual sequencing methods, which are well known in the art. An error in a sequence which results in an insertion or deletion of one or more nucleotides may result in a frame shift in translation such that the predicted amino acid sequence will differ from that which would be predicted from the actual nucleotide sequence of the nucleic acid molecule, starting at the point of the mutation.

The nucleic acid molecules of the present invention, and fragments derived therefrom, are useful for screening for restriction fragment length polymorphism (RFLP) associated with certain disorders, as well as for genetic mapping.

The polynucleotide sequence information provided by the invention makes possible large-scale expression of the encoded polypeptide by techniques well known and routinely practiced in the art.

Vectors

Another aspect of the present invention is directed to vectors, or recombinant expression vectors, comprising any of the nucleic acid molecules described above. Vectors are used herein either to amplify DNA or RNA encoding nGPCR-x and/or to express DNA which encodes nGPCR-x. Preferred vectors include, but are not limited to, plasmids, phages, cosmids, episomes, viral particles or viruses, and integratable DNA fragments (*i.e.*, fragments integratable into the host genome by homologous recombination). Preferred viral particles include, but are not limited to, adenoviruses, baculoviruses, parvoviruses, herpesviruses, poxviruses, adeno-associated viruses, Semliki Forest viruses, vaccinia viruses, and retroviruses. Preferred expression vectors include, but are not limited to, pcDNA3 (Invitrogen) and pSVL (Pharmacia Biotech). Other expression vectors include, but are not limited to, pSPORT™ vectors, pGEM™ vectors (Promega), pPROEXvectors™ (LTI, Bethesda, MD), Bluescript™ vectors (Stratagene), pQE™ vectors (Qiagen), pSE420™ (Invitrogen), and pYES2™(Invitrogen).

Expression constructs preferably comprise GPCR-x-encoding polynucleotides operatively linked to an endogenous or exogenous expression control DNA sequence and a transcription terminator. Expression control DNA sequences include promoters, enhancers, operators, and regulatory element binding sites generally, and are typically selected based on the expression systems in which the expression construct is to be utilized. Preferred promoter and enhancer sequences are generally selected for the ability to increase gene expression, while operator sequences are generally selected for the ability to regulate gene expression. Expression constructs of the invention may also include sequences encoding one or more selectable markers that permit identification of host cells bearing the construct. Expression constructs may also include sequences that facilitate, and preferably promote, homologous recombination in a host cell. Preferred constructs of the invention also include sequences necessary for replication in a host cell.

Expression constructs are preferably utilized for production of an encoded protein, but may also be utilized simply to amplify a nGPCR-x-encoding polynucleotide sequence.

In preferred embodiments, the vector is an expression vector wherein the polynucleotide of the invention is operatively linked to a polynucleotide comprising an expression control sequence. Autonomously replicating recombinant expression constructs such as plasmid and viral DNA vectors incorporating polynucleotides of the invention are also provided. Preferred expression vectors are replicable DNA constructs in which a DNA sequence encoding nGPCR-x is operably linked or connected to suitable control sequences capable of effecting the expression of the nGPCR-x in a suitable host. DNA regions are operably linked or connected when they are functionally related to each other. For example, a promoter is operably linked or connected to a coding sequence if it controls the transcription of the sequence. Amplification vectors do not require expression control domains, but rather need only the ability to replicate in a host, usually conferred by an origin of replication, and a selection gene to facilitate recognition of transformants. The need for control sequences in the expression vector will vary depending upon the host selected and the transformation method chosen. Generally, control sequences include a transcriptional promoter, an optional operator sequence to control transcription, a sequence encoding suitable mRNA ribosomal binding and sequences which control the termination of transcription and translation.

Preferred vectors preferably contain a promoter that is recognized by the host organism. The promoter sequences of the present invention may be prokaryotic, eukaryotic or viral. Examples of suitable prokaryotic sequences include the P_R and P_L promoters of bacteriophage lambda (The bacteriophage Lambda, Hershey, A. D., Ed., Cold Spring Harbor Press, Cold Spring Harbor, NY (1973), which is incorporated herein by reference in its entirety; Lambda II, Hendrix, R. W., Ed., Cold Spring Harbor Press, Cold Spring Harbor, NY (1980), which is incorporated herein by reference in its entirety); the trp, recA, heat shock, and lacZ promoters of *E. coli* and the SV40 early promoter (Benoist *et al. Nature*, 1981, *290*, 304-310, which is incorporated herein by reference in its entirety). Additional promoters include, but are not limited to, mouse mammary tumor virus, long terminal repeat of human immunodeficiency virus, maloney virus, cytomegalovirus immediate early promoter, Epstein Barr virus, Rous sarcoma virus, human actin, human myosin, human hemoglobin, human muscle creatine, and human metalothionein.

Additional regulatory sequences can also be included in preferred vectors. Preferred examples of suitable regulatory sequences are represented by the Shine-Dalgarno of the replicase gene of the phage MS-2 and of the gene cII of bacteriophage lambda. The Shine-Dalgarno sequence may be directly followed by DNA encoding nGPCR-x and result in the expression of the mature nGPCR-x protein.

Moreover, suitable expression vectors can include an appropriate marker that allows the screening of the transformed host cells. The transformation of the selected host is carried out using any one of the various techniques well known to the expert in the art and described in Sambrook *et al., supra.*

An origin of replication can also be provided either by construction of the vector to include an exogenous origin or may be provided by the host cell chromosomal replication mechanism. If the vector is integrated into the host cell chromosome, the latter may be sufficient. Alternatively, rather than using vectors which contain viral origins of replication, one skilled in the art can transform mammalian cells by the method of co-transformation with a selectable marker and nGPCR-x DNA. An example of a suitable marker is dihydrofolate reductase (DHFR) or thymidine kinase (*see*, U.S. Patent No. 4,399,216).

Nucleotide sequences encoding GPCR-x may be recombined with vector DNA in accordance with conventional techniques, including blunt-ended or staggered-ended termini for ligation, restriction enzyme digestion to provide appropriate termini, filling in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesiderable joining, and ligation with appropriate ligases. Techniques for such manipulation are disclosed by Sambrook et al., *supra* and are well known in the art. Methods for construction of mammalian expression vectors are disclosed in, for example, Okayama *et al., Mol. Cell. Biol.*, **1983**, *3*, 280, Cosman *et al., Mol. Immunol.*, **1986**, *23*, 935, Cosman *et al., Nature*, **1984**, *312*, 768, EP-A-0367566, and WO 91/18982, each of which is incorporated herein by reference in its entirety.

Host cells

According to another aspect of the invention, host cells are provided, including prokaryotic and eukaryotic cells, comprising a polynucleotide of the invention (or vector of the invention) in a manner that permits expression of the encoded nGPCR-x

polypeptide. Polynucleotides of the invention may be introduced into the host cell as part of a circular plasmid, or as linear DNA comprising an isolated protein coding region or a viral vector. Methods for introducing DNA into the host cell that are well known and routinely practiced in the art include transformation, transfection, electroporation, nuclear injection, or fusion with carriers such as liposomes, micelles, ghost cells, and protoplasts. Expression systems of the invention include bacterial, yeast, fungal, plant, insect, invertebrate, vertebrate, and mammalian cells systems.

The invention provides host cells that are transformed or transfected (stably or transiently) with polynucleotides of the invention or vectors of the invention. As stated above, such host cells are useful for amplifying the polynucleotides and also for expressing the nGPCR-x polypeptide or fragment thereof encoded by the polynucleotide.

In still another related embodiment, the invention provides a method for producing a nGPCR-x polypeptide (or fragment thereof) comprising the steps of growing a host cell of the invention in a nutrient medium and isolating the polypeptide or variant thereof from the cell or the medium. Because nGPCR-x is a seven transmembrane receptor, it will be appreciated that, for some applications, such as certain activity assays, the preferable isolation may involve isolation of cell membranes containing the polypeptide embedded therein, whereas for other applications a more complete isolation may be preferable.

According to some aspects of the present invention, transformed host cells having an expression vector comprising any of the nucleic acid molecules described above are provided. Expression of the nucleotide sequence occurs when the expression vector is introduced into an appropriate host cell. Suitable host cells for expression of the polypeptides of the invention include, but are not limited to, prokaryotes, yeast, and eukaryotes. If a prokaryotic expression vector is employed, then the appropriate host cell would be any prokaryotic cell capable of expressing the cloned sequences. Suitable prokaryotic cells include, but are not limited to, bacteria of the genera *Escherichia*, *Bacillus*, *Salmonella*, *Pseudomonas*, *Streptomyces*, and *Staphylococcus*.

If an eukaryotic expression vector is employed, then the appropriate host cell would be any eukaryotic cell capable of expressing the cloned sequence. Preferably, eukaryotic cells are cells of higher eukaryotes. Suitable eukaryotic cells include, but are not limited to, non-human mammalian tissue culture cells and human tissue culture cells.

Preferred host cells include, but are not limited to, insect cells, HeLa cells, Chinese hamster ovary cells (CHO cells), African green monkey kidney cells (COS cells), human HEK-293 cells, and murine 3T3 fibroblasts. Propagation of such cells in cell culture has become a routine procedure (*see*, Tissue Culture, Academic Press, Kruse and Patterson, eds. (1973), which is incorporated herein by reference in its entirety).

In addition, a yeast host may be employed as a host cell. Preferred yeast cells include, but are not limited to, the genera *Saccharomyces*, *Pichia*, and *Kluveromyces*. Preferred yeast hosts are *S. cerevisiae* and *P. pastoris*. Preferred yeast vectors can contain an origin of replication sequence from a 2T yeast plasmid, an autonomously replication sequence (ARS), a promoter region, sequences for polyadenylation, sequences for transcription termination, and a selectable marker gene. Shuttle vectors for replication in both yeast and *E. coli* are also included herein.

Alternatively, insect cells may be used as host cells. In a preferred embodiment, the polypeptides of the invention are expressed using a baculovirus expression system (*see*, Luckow *et al.*, *Bio/Technology*, **1988**, *6*, 47, Baculovirus Expression Vectors: A Laboratory Manual, O'Rielly *et al.* (Eds.), W.H. Freeman and Company, New York, **1992**, and U.S. Patent No. 4,879,236, each of which is incorporated herein by reference in its entirety). In addition, the MAXBAC™ complete baculovirus expression system (Invitrogen) can, for example, be used for production in insect cells.

Host cells of the invention are a valuable source of immunogen for development of antibodies specifically immunoreactive with nGPCR-x. Host cells of the invention are also useful in methods for the large-scale production of nGPCR-x polypeptides wherein the cells are grown in a suitable culture medium and the desired polypeptide products are isolated from the cells, or from the medium in which the cells are grown, by purification methods known in the art, *e.g.*, conventional chromatographic methods including immunoaffinity chromatography, receptor affinity chromatography, hydrophobic interaction chromatography, lectin affinity chromatography, size exclusion filtration, cation or anion exchange chromatography, high pressure liquid chromatography (HPLC), reverse phase HPLC, and the like. Still other methods of purification include those methods wherein the desired protein is expressed and purified as a fusion protein having a specific tag, label, or chelating moiety that is recognized by a specific binding partner or

agent. The purified protein can be cleaved to yield the desired protein, or can be left as an intact fusion protein. Cleavage of the fusion component may produce a form of the desired protein having additional amino acid residues as a result of the cleavage process.

Knowledge of nGPCR-x DNA sequences allows for modification of cells to permit, or increase, expression of endogenous nGPCR-x. Cells can be modified (*e.g*, by homologous recombination) to provide increased expression by replacing, in whole or in part, the naturally occurring nGPCR-x promoter with all or part of a heterologous promoter so that the cells express nGPCR-x at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to endogenous nGPCR-x encoding sequences. (See, for example, PCT International Publication No. WO 94/12650, PCT International Publication No. WO 92/20808, and PCT International Publication No. WO 91/09955.) It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (*e.g.*, ada, dhfr, and the multifunctional CAD gene which encodes carbamoyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If linked to the nGPCR-x coding sequence, amplification of the marker DNA by standard selection methods results in co-amplification of the nGPCR-x coding sequences in the cells.

Knock-outs

The DNA sequence information provided by the present invention also makes possible the development (*e.g.*, by homologous recombination or "knock-out" strategies; see Capecchi, *Science 244*:1288-1292 (1989), which is incorporated herein by reference) of animals that fail to express functional nGPCR-x or that express a variant of nGPCR-x. Such animals (especially small laboratory animals such as rats, rabbits, and mice) are useful as models for studying the *in vivo* activities of nGPCR-x and modulators of nGPCR-x.

Antisense

Also made available by the invention are anti-sense polynucleotides that recognize and hybridize to polynucleotides encoding nGPCR-x. Full-length and fragment anti-sense polynucleotides are provided. Fragment antisense molecules of the invention include (i) those that specifically recognize and hybridize to nGPCR-x RNA (as determined by sequence comparison of DNA encoding nGPCR-x to DNA encoding other known

molecules). Identification of sequences unique to nGPCR-x encoding polynucleotides can be deduced through use of any publicly available sequence database, and/or through use of commercially available sequence comparison programs. After identification of the desired sequences, isolation through restriction digestion or amplification using any of the various polymerase chain reaction techniques well known in the art can be performed. Anti-sense polynucleotides are particularly relevant to regulating expression of nGPCR-x by those cells expressing nGPCR-x mRNA.

Antisense nucleic acids (preferably 10 to 30 base-pair oligonucleotides) capable of specifically binding to nGPCR-x expression control sequences or nGPCR-x RNA are introduced into cells (*e.g.*, by a viral vector or colloidal dispersion system such as a liposome). The antisense nucleic acid binds to the nGPCR-x target nucleotide sequence in the cell and prevents transcription and/or translation of the target sequence. Phosphorothioate and methylphosphonate antisense oligonucleotides are specifically contemplated for therapeutic use by the invention. The antisense oligonucleotides may be further modified by adding poly-L-lysine, transferrin polylysine, or cholesterol moieties at their 5' end. Suppression of nGPCR-x expression at either the transcriptional or translational level is useful to generate cellular or animal models for diseases/conditions characterized by aberrant nGPCR-x expression.

Antisense oligonucleotides, or fragments of sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, or sequences complementary or homologous thereto, derived from the nucleotide sequences of the present invention encoding nGPCR-x are useful as diagnostic tools for probing gene expression in various tissues. For example, tissue can be probed *in situ* with oligonucleotide probes carrying detectable groups by conventional autoradiography techniques to investigate native expression of this enzyme or pathological conditions relating thereto. Antisense oligonucleotides are preferably directed to regulatory regions of sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, or mRNA corresponding thereto, including, but not limited to, the initiation codon, TATA box, enhancer sequences, and the like.

Transcription factors

The nGPCR-x sequences taught in the present invention facilitate the design of novel transcription factors for modulating nGPCR-x expression in native cells and animals, and cells transformed or transfected with nGPCR-x polynucleotides. For example, the Cys_2-His_2 zinc finger proteins, which bind DNA via their zinc finger domains, have been shown to be amenable to structural changes that lead to the recognition of different target sequences. These artificial zinc finger proteins recognize specific target sites with high affinity and low dissociation constants, and are able to act as gene switches to modulate gene expression. Knowledge of the particular nGPCR-x target sequence of the present invention facilitates the engineering of zinc finger proteins specific for the target sequence using known methods such as a combination of structure-based modeling and screening of phage display libraries (Segal *et al.*, Proc. Natl. Acad. Sci. (USA) 96:2758-2763 (1999); Liu *et al.*, Proc. Natl. Acad. Sci. (USA) 94:5525-5530 (1997); Greisman *et al.*, Science 275:657-661 (1997); Choo *et al.*, J. Mol. Biol. 273:525-532 (1997)). Each zinc finger domain usually recognizes three or more base pairs. Since a recognition sequence of 18 base pairs is generally sufficient in length to render it unique in any known genome, a zinc finger protein consisting of 6 tandem repeats of zinc fingers would be expected to ensure specificity for a particular sequence (Segal *et al.*) The artificial zinc finger repeats, designed based on nGPCR-x sequences, are fused to activation or repression domains to promote or suppress nGPCR-x expression (Liu *et al.)* Alternatively, the zinc finger domains can be fused to the TATA box-binding factor (TBP) with varying lengths of linker region between the zinc finger peptide and the TBP to create either transcriptional activators or repressors (Kim *et al.*, Proc. Natl. Acad. Sci. (USA) 94:3616-3620 (1997). Such proteins and polynucleotides that encode them, have utility for modulating nGPCR-x expression *in vivo* in both native cells, animals and humans; and/or cells transfected with nGPCR-x-encoding sequences. The novel transcription factor can be delivered to the target cells by transfecting constructs that express the transcription factor (gene therapy), or by introducing the protein. Engineered zinc finger proteins can also be designed to bind RNA sequences for use in therapeutics as alternatives to antisense or catalytic RNA methods (McColl *et al.*, Proc. Natl. Acad. Sci. (USA) 96:9521-9526 (1997); Wu *et al.*, Proc. Natl. Acad. Sci. (USA) 92:344-348 (1995)). The present invention contemplates methods of designing such transcription factors based

on the gene sequence of the invention, as well as customized zinc finger proteins, that are useful to modulate nGPCR-x expression in cells (native or transformed) whose genetic complement includes these sequences.

Polypeptides

The invention also provides purified and isolated mammalian nGPCR-x polypeptides encoded by a polynucleotide of the invention. Presently preferred is a human nGPCR-x polypeptide comprising the amino acid sequence set out in sequences selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, or fragments thereof comprising an epitope specific to the polypeptide. By "epitope specific to" is meant a portion of the nGPCR receptor that is recognizable by an antibody that is specific for the nGPCR, as defined in detail below.

Although the sequences provided are particular human sequences, the invention is intended to include within its scope other human allelic variants; non-human mammalian forms of nGPCR-x, and other vertebrate forms of nGPCR-x.

It will be appreciated that extracellular epitopes are particularly useful for generating and screening for antibodies and other binding compounds that bind to receptors such as nGPCR-x. Thus, in another preferred embodiment, the invention provides a purified and isolated polypeptide comprising at least one extracellular domain (*e.g.*, the N-terminal extracellular domain or one of the three extracellular loops) of nGPCR-x. Purified and isolated polypeptides comprising the N-terminal extracellular domain of nGPCR-x are highly preferred. Also preferred is a purified and isolated polypeptide comprising a nGPCR-x fragment selected from the group consisting of the N-terminal extracellular domain of nGPCR-x, transmembrane domains of nGPCR-x, an extracellular loop connecting transmembrane domains of nGPCR-x, an intracellular loop connecting transmembrane domains of nGPCR-x, the C-terminal cytoplasmic region of nGPCR-x, and fusions thereof. Such fragments may be continuous portions of the native receptor. However, it will also be appreciated that knowledge of the nGPCR-x gene and protein sequences as provided herein permits recombining of various domains that are not contiguous in the native protein. Using a FORTRAN computer program called "tmtrest.all" [Parodi *et al.*, Comput. Appl. Biosci. 5:527-535 (1994)], nGPCR-x was shown to contain transmembrane-spanning domains.

The invention also embraces polypeptides that have at least 99%, at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55% or at least 50% identity and/or homology to the preferred polypeptide of the invention. Percent amino acid sequence "identity" with respect to the preferred polypeptide of the invention is defined herein as the percentage of amino acid residues in the candidate sequence that are identical with the residues in the nGPCR-x sequence after aligning both sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Percent sequence "homology" with respect to the preferred polypeptide of the invention is defined herein as the percentage of amino acid residues in the candidate sequence that are identical with the residues in the nGPCR-x sequence after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and also considering any conservative substitutions as part of the sequence identity.

In one aspect, percent homology is calculated as the percentage of amino acid residues in the smaller of two sequences which align with identical amino acid residue in the sequence being compared, when four gaps in a length of 100 amino acids may be introduced to maximize alignment (Dayhoff, in Atlas of Protein Sequence and Structure, Vol. 5, p. 124, National Biochemical Research Foundation, Washington, D.C. (1972), incorporated herein by reference).

Polypeptides of the invention may be isolated from natural cell sources or may be chemically synthesized, but are preferably produced by recombinant procedures involving host cells of the invention. Use of mammalian host cells is expected to provide for such post-translational modifications (*e.g.*, glycosylation, truncation, lipidation, and phosphorylation) as may be needed to confer optimal biological activity on recombinant expression products of the invention. Glycosylated and non-glycosylated forms of nGPCR-x polypeptides are embraced by the invention.

The invention also embraces variant (or analog) nGPCR-x polypeptides. In one example, insertion variants are provided wherein one or more amino acid residues supplement a nGPCR-x amino acid sequence. Insertions may be located at either or both termini of the protein, or may be positioned within internal regions of the nGPCR-x amino

acid sequence. Insertional variants with additional residues at either or both termini can include, for example, fusion proteins and proteins including amino acid tags or labels.

Insertion variants include nGPCR-x polypeptides wherein one or more amino acid residues are added to a nGPCR-x acid sequence or to a biologically active fragment thereof.

Variant products of the invention also include mature nGPCR-x products, *i.e.*, nGPCR-x products wherein leader or signal sequences are removed, with additional amino terminal residues. The additional amino terminal residues may be derived from another protein, or may include one or more residues that are not identifiable as being derived from specific proteins. nGPCR-x products with an additional methionine residue at position -1 (Met^{-1}-nGPCR-x) are contemplated, as are variants with additional methionine and lysine residues at positions -2 and -1 (Met^{-2}-Lys^{-1}-nGPCR-x). Variants of nGPCR-x with additional Met, Met-Lys, Lys residues (or one or more basic residues in general) are particularly useful for enhanced recombinant protein production in bacterial host cells.

The invention also embraces nGPCR-x variants having additional amino acid residues that result from use of specific expression systems. For example, use of commercially available vectors that express a desired polypeptide as part of a glutathione-S-transferase (GST) fusion product provides the desired polypeptide having an additional glycine residue at position -1 after cleavage of the GST component from the desired polypeptide. Variants that result from expression in other vector systems are also contemplated.

Insertional variants also include fusion proteins wherein the amino terminus and/or the carboxy terminus of nGPCR-x is/are fused to another polypeptide.

In another aspect, the invention provides deletion variants wherein one or more amino acid residues in a nGPCR-x polypeptide are removed. Deletions can be effected at one or both termini of the nGPCR-x polypeptide, or with removal of one or more non-terminal amino acid residues of nGPCR-x. Deletion variants, therefore, include all fragments of a nGPCR-x polypeptide.

The invention also embraces polypeptide fragments of sequences selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, wherein the fragments maintain

biological (*e.g.*, ligand binding and/or intracellular signaling) immunological properties of a nGPCR-x polypeptide.

In one preferred embodiment of the invention, an isolated nucleic acid molecule comprises a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence homologous to sequences selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, and fragments thereof, wherein the nucleic acid molecule encoding at least a portion of nGPCR-x. In a more preferred embodiment, the isolated nucleic acid molecule comprises a sequence that encodes a polypeptide comprising sequences selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, and fragments thereof.

As used in the present invention, polypeptide fragments comprise at least 5, 10, 15, 20, 25, 30, 35, or 40 consecutive amino acids of sequences selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268. Preferred polypeptide fragments display antigenic properties unique to, or specific for, human nGPCR-x and its allelic and species homologs. Fragments of the invention having the desired biological and immunological properties can be prepared by any of the methods well known and routinely practiced in the art.

In still another aspect, the invention provides substitution variants of nGPCR-x polypeptides. Substitution variants include those polypeptides wherein one or more amino acid residues of a nGPCR-x polypeptide are removed and replaced with alternative residues. In one aspect, the substitutions are conservative in nature; however, the invention embraces substitutions that are also non-conservative. Conservative substitutions for this purpose may be defined as set out in Tables 2, 3, or 4 below.

Variant polypeptides include those wherein conservative substitutions have been introduced by modification of polynucleotides encoding polypeptides of the invention. Amino acids can be classified according to physical properties and contribution to secondary and tertiary protein structure. A conservative substitution is recognized in the art as a substitution of one amino acid for another amino acid that has similar properties. Exemplary conservative substitutions are set out in Table 2 (from WO 97/09433, page 10, published March 13, 1997 (PCT/GB96/02197, filed 9/6/96), immediately below.

Table 2

Conservative Substitutions I

SIDE CHAIN CHARACTERISTIC	AMINO ACID
Aliphatic	
Non-polar	G A P
	I L V
Polar - uncharged	C S T M
	N Q
Polar - charged	D E
	K R
Aromatic	H F W Y
Other	N Q D E

Alternatively, conservative amino acids can be grouped as described in Lehninger, [Biochemistry, Second Edition; Worth Publishers, Inc. NY, NY (1975), pp.71-77] as set out in Table 3, below.

Table 3
Conservative Substitutions II

SIDE CHAIN CHARACTERISTIC	AMINO ACID
Non-polar (hydrophobic)	
A. Aliphatic:	A L I V P
B. Aromatic:	F W
C. Sulfur-containing:	M
D. Borderline:	G
Uncharged-polar	
A. Hydroxyl:	S T Y
B. Amides:	N Q
C. Sulfhydryl:	C
D. Borderline:	G
Positively Charged (Basic):	K R H
Negatively Charged (Acidic):	D E

As still another alternative, exemplary conservative substitutions are set out in Table 4, below.

Table 4
Conservative Substitutions III

Original Residue	Exemplary Substitution
Ala (A)	Val, Leu, Ile
Arg (R)	Lys, Gln, Asn
Asn (N)	Gln, His, Lys, Arg
Asp (D)	Glu
Cys (C)	Ser
Gln (Q)	Asn
Glu (E)	Asp
His (H)	Asn, Gln, Lys, Arg

Ile (I)	Leu, Val, Met, Ala, Phe,
Leu (L)	Ile, Val, Met, Ala, Phe
Lys (K)	Arg, Gln, Asn
Met (M)	Leu, Phe, Ile
Phe (F)	Leu, Val, Ile, Ala
Pro (P)	Gly
Ser (S)	Thr
Thr (T)	Ser
Trp (W)	Tyr
Tyr (Y)	Trp, Phe, Thr, Ser
Val (V)	Ile, Leu, Met, Phe, Ala

It should be understood that the definition of polypeptides of the invention is intended to include polypeptides bearing modifications other than insertion, deletion, or substitution of amino acid residues. By way of example, the modifications may be covalent in nature, and include for example, chemical bonding with polymers, lipids, other organic, and inorganic moieties. Such derivatives may be prepared to increase circulating half-life of a polypeptide, or may be designed to improve the targeting capacity of the polypeptide for desired cells, tissues, or organs. Similarly, the invention further embraces nGPCR-x polypeptides that have been covalently modified to include one or more water-soluble polymer attachments such as polyethylene glycol, polyoxyethylene glycol, or polypropylene glycol. Variants that display ligand binding properties of native nGPCR-x and are expressed at higher levels, as well as variants that provide for constitutively active receptors, are particularly useful in assays of the invention; the variants are also useful in providing cellular, tissue and animal models of diseases/conditions characterized by aberrant nGPCR-x activity.

In a related embodiment, the present invention provides compositions comprising purified polypeptides of the invention. Preferred compositions comprise, in addition to the polypeptide of the invention, a pharmaceutically acceptable (*i.e.,* sterile and non-toxic) liquid, semisolid, or solid diluent that serves as a pharmaceutical vehicle, excipient, or medium. Any diluent known in the art may be used. Exemplary diluents include, but are not limited to, water, saline solutions, polyoxyethylene sorbitan monolaurate, magnesium stearate, methyl- and propylhydroxybenzoate, talc, alginates, starches, lactose, sucrose, dextrose, sorbitol, mannitol, glycerol, calcium phosphate, mineral oil, and cocoa butter.

Variants that display ligand binding properties of native nGPCR-x and are expressed at higher levels, as well as variants that provide for constitutively active receptors, are particularly useful in assays of the invention; the variants are also useful in assays of the invention and in providing cellular, tissue and animal models of diseases/conditions characterized by aberrant nGPCR-x activity.

The G protein-coupled receptor functions through a specific heterotrimeric guanine-nucleotide-binding regulatory protein (G-protein) coupled to the intracellular portion of the G protein-coupled receptor molecule. Accordingly, the G protein-coupled receptor has a specific affinity to G protein. G proteins specifically bind to guanine nucleotides. Isolation of G proteins provides a means to isolate guanine nucleotides. G proteins may be isolated using commercially available anti-G protein antibodies or isolated G protein-coupled receptors. Similarly, G proteins may be detected in a sample isolated using commercially available detectable anti-G protein antibodies or isolated G protein-coupled receptors.

According to the present invention, the isolated nGPCR-x proteins of the present invention are useful to isolate and purify G proteins from samples such as cell lysates. Example 15 below sets forth an example of isolation of G proteins using isolated nGPCR-x proteins. Such methodolgy may be used in place of the use of commercially available anti-G protein antibodies which are used to isolate G proteins. Moreover, G proteins may be detected using n-GPCR-x proteins in place of commercially available detectable anti-G protein antibodies. Since nGPCR-x proteins specifically bind to G proteins, they can be employed in any specific use where G protein specific affinity is required such as those uses where commercially available anti-G protein antibodies are employed.

Antibodies

Also comprehended by the present invention are antibodies (*e.g.*, monoclonal and polyclonal antibodies, single chain antibodies, chimeric antibodies, bifunctional/bispecific antibodies, humanized antibodies, human antibodies, and complementary determining region (CDR)-grafted antibodies, including compounds which include CDR sequences which specifically recognize a polypeptide of the invention) specific for nGPCR-x or fragments thereof. Preferred antibodies of the invention are human antibodies that are produced and identified according to methods described in WO93/11236, published June

20, 1993, which is incorporated herein by reference in its entirety. Antibody fragments, including Fab, Fab′, F(ab′)$_2$, and F_v, are also provided by the invention. The term "specific for," when used to describe antibodies of the invention, indicates that the variable regions of the antibodies of the invention recognize and bind nGPCR-x polypeptides exclusively (*i.e.*, are able to distinguish nGPCR-x polypeptides from other known GPCR polypeptides by virtue of measurable differences in binding affinity, despite the possible existence of localized sequence identity, homology, or similarity between nGPCR-x and such polypeptides). It will be understood that specific antibodies may also interact with other proteins (for example, *S. aureus* protein A or other antibodies in ELISA techniques) through interactions with sequences outside the variable region of the antibodies, and, in particular, in the constant region of the molecule. Screening assays to determine binding specificity of an antibody of the invention are well known and routinely practiced in the art. For a comprehensive discussion of such assays, see Harlow *et al.* (Eds.), Antibodies A Laboratory Manual; Cold Spring Harbor Laboratory; Cold Spring Harbor, NY (1988), Chapter 6. Antibodies that recognize and bind fragments of the nGPCR-x polypeptides of the invention are also contemplated, provided that the antibodies are specific for nGPCR-x polypeptides. Antibodies of the invention can be produced using any method well known and routinely practiced in the art.

The invention provides an antibody that is specific for the nGPCR-x of the invention. Antibody specificity is described in greater detail below. However, it should be emphasized that antibodies that can be generated from polypeptides that have previously been described in the literature and that are capable of fortuitously cross-reacting with nGPCR-x (*e.g.*, due to the fortuitous existence of a similar epitope in both polypeptides) are considered "cross-reactive" antibodies. Such cross-reactive antibodies are not antibodies that are "specific" for nGPCR-x. The determination of whether an antibody is specific for nGPCR-x or is cross-reactive with another known receptor is made using any of several assays, such as Western blotting assays, that are well known in the art. For identifying cells that express nGPCR-x and also for modulating nGPCR-x-ligand binding activity, antibodies that specifically bind to an extracellular epitope of the nGPCR-x are preferred.

In one preferred variation, the invention provides monoclonal antibodies. Hybridomas that produce such antibodies also are intended as aspects of the invention. In yet another variation, the invention provides a humanized antibody. Humanized antibodies are useful for *in vivo* therapeutic indications.

In another variation, the invention provides a cell-free composition comprising polyclonal antibodies, wherein at least one of the antibodies is an antibody of the invention specific for nGPCR-x. Antisera isolated from an animal is an exemplary composition, as is a composition comprising an antibody fraction of an antisera that has been resuspended in water or in another diluent, excipient, or carrier.

In still another related embodiment, the invention provides an anti-idiotypic antibody specific for an antibody that is specific for nGPCR-x.

It is well known that antibodies contain relatively small antigen binding domains that can be isolated chemically or by recombinant techniques. Such domains are useful nGPCR-x binding molecules themselves, and also may be reintroduced into human antibodies, or fused to toxins or other polypeptides. Thus, in still another embodiment, the invention provides a polypeptide comprising a fragment of a nGPCR-x-specific antibody, wherein the fragment and the polypeptide bind to the nGPCR-x. By way of non-limiting example, the invention provides polypeptides that are single chain antibodies and CDR-grafted antibodies.

Non-human antibodies may be humanized by any of the methods known in the art. In one method, the non-human CDRs are inserted into a human antibody or consensus antibody framework sequence. Further changes can then be introduced into the antibody framework to modulate affinity or immunogenicity.

Antibodies of the invention are useful for, *e.g.*, therapeutic purposes (by modulating activity of nGPCR-x), diagnostic purposes to detect or quantitate nGPCR-x, and purification of nGPCR-x. Kits comprising an antibody of the invention for any of the purposes described herein are also comprehended. In general, a kit of the invention also includes a control antigen for which the antibody is immunospecific.

Compositions

Mutations in the nGPCR-x gene that result in loss of normal function of the nGPCR-x gene product underlie nGPCR-x-related human disease states. The invention

comprehends gene therapy to restore nGPCR-x activity to treat those disease states. Delivery of a functional nGPCR-x gene to appropriate cells is effected *ex vivo, in situ*, or *in vivo* by use of vectors, and more particularly viral vectors (*e.g*, adenovirus, adeno-associated virus, or a retrovirus), or *ex vivo* by use of physical DNA transfer methods (*e.g.*, liposomes or chemical treatments). See, for example, Anderson, *Nature*, supplement to vol. 392, no. 6679, pp.25-20 (1998). For additional reviews of gene therapy technology see Friedmann, *Science, 244*: 1275-1281 (1989); Verma, *Scientific American*: 68-84 (1990); and Miller, *Nature, 357*: 455-460 (1992). Alternatively, it is contemplated that in other human disease states, preventing the expression of, or inhibiting the activity of, nGPCR-x will be useful in treating disease states. It is contemplated that antisense therapy or gene therapy could be applied to negatively regulate the expression of nGPCR-x.

Another aspect of the present invention is directed to compositions, including pharmaceutical compositions, comprising any of the nucleic acid molecules or recombinant expression vectors described above and an acceptable carrier or diluent. Preferably, the carrier or diluent is pharmaceutically acceptable. Suitable carriers are described in the most recent edition of *Remington's Pharmaceutical Sciences*, A. Osol, a standard reference text in this field, which is incorporated herein by reference in its entirety. Preferred examples of such carriers or diluents include, but are not limited to, water, saline, Ringer's solution, dextrose solution, and 5% human serum albumin. Liposomes and nonaqueous vehicles such as fixed oils may also be used. The formulations are sterilized by commonly used techniques.

Also within the scope of the invention are compositions comprising polypeptides, polynucleotides, or antibodies of the invention that have been formulated with, *e.g.*, a pharmaceutically acceptable carrier.

The invention also provides methods of using antibodies of the invention. For example, the invention provides a method for modulating ligand binding of a nGPCR-x comprising the step of contacting the nGPCR-x with an antibody specific for the nGPCR-x, under conditions wherein the antibody binds the receptor.

As discussed above, it is well known that GPCRs are expressed in many different tissues and regions, including in the brain. GPCRs that may be expressed in the brain, such as nGPCR-x, provide an indication that aberrant nGPCR-x signaling activity may

correlate with one or more neurological or psychological disorders. The invention also provides a method for treating a neurological or psychiatric disorder comprising the step of administering to a mammal in need of such treatment an amount of an antibody-like polypeptide of the invention that is sufficient to modulate ligand binding to a nGPCR-x in neurons of the mammal. nGPCR-x may also be expressed in other tissues, including but not limited to, peripheral blood lymphocytes, pancreas, ovary, uterus, testis, salivary gland, thyroid gland, kidney, adrenal gland, liver, bone marrow, prostate, fetal liver, colon, muscle, and fetal brain, and may be found in many other tissues. Within the brain, nGPCR-x mRNA transcripts may be found in many tissues, including, but not limited to, frontal lobe, hypothalamus, pons, cerebellum, caudate nucleus, and medulla.

Kits

The present invention is also directed to kits, including pharmaceutical kits. The kits can comprise any of the nucleic acid molecules described above, any of the polypeptides described above, or any antibody which binds to a polypeptide of the invention as described above, as well as a negative control. The kit preferably comprises additional components, such as, for example, instructions, solid support, reagents helpful for quantification, and the like.

In another aspect, the invention features methods for detection of a polypeptide in a sample as a diagnostic tool for diseases or disorders, wherein the method comprises the steps of: (a) contacting the sample with a nucleic acid probe which hybridizes under hybridization assay conditions to a nucleic acid target region of a polypeptide having sequences selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, said probe comprising the nucleic acid sequence encoding the polypeptide, fragments thereof, and the complements of the sequences and fragments; and (b) detecting the presence or amount of the probe:target region hybrid as an indication of the disease.

In preferred embodiments of the invention, the disease is selected from the group consisting of thyroid disorders (*e.g.* thyreotoxicosis, myxoedema); renal failure; inflammatory conditions (*e.g.*, Crohn's disease); diseases related to cell differentiation and homeostasis; rheumatoid arthritis; autoimmune disorders; movement disorders; CNS disorders (*e.g.*, pain including migraine; stroke; psychotic and neurological disorders, including anxiety, mental disorder, manic depression, anxiety, generalized anxiety

disorder, post-traumatic-stress disorder, depression, bipolar disorder, delirium, dementia, severe mental retardation; dyskinesias, such as Huntington's disease or Tourette's Syndrome; attention disorders including ADD and ADHD, and degenerative disorders such as Parkinson's, Alzheimer's; movement disorders, including ataxias, supranuclear palsy, *etc.*); infections, such as viral infections caused by HIV-1 or HIV-2; metabolic and cardiovascular diseases and disorders (*e.g.*, type 2 diabetes, impaired glucose tolerance, dyslipidemia, obesity, anorexia, hypotension, hypertension, thrombosis, myocardial infarction, cardiomyopathies, atherosclerosis, *etc.*); proliferative diseases and cancers (*e.g.*, different cancers such as breast, colon, lung, *etc.*, and hyperproliferative disorders such as psoriasis, prostate hyperplasia, *etc.*); hormonal disorders (*e.g.*, male/female hormonal replacement, polycystic ovarian syndrome, alopecia, *etc.*); and sexual dysfunction, among others.

As described above and in Example 5 below, the gene encoding nGPCR-74 (nucleic acid sequence SEQ ID NO:134, amino acid sequence SEQ ID NO:268) has been detected in brain tissue indicating that this nGPCR protein is a neuroreceptor. It is well known that other nGPCR-x are expressed in many different tissues, including the brain. Accordingly, the nGPCR-x of the present invention may be useful, *inter alia*, for treating and/or diagnosing mental disorders. Following the techniques described in Example 5, below, those skilled in the art could readily ascertain if nGPCR-x is expressed in a particular tissue or region.

Kits may be designed to detect either expression of polynucleotides encoding nGPCR-x expressed in the brain or the nGPCR-x proteins themselves in order to identify tissue as being neurological. For example, oligonucleotide hybridization kits can be provided which include a container having an oligonucleotide probe specific for the nGPCR-x-specific DNA and optionally, containers with positive and negative controls and/or instructions. Similarly, PCR kits can be provided which include a container having primers specific for the nGPCR-x-specific sequences, DNA and optionally, containers with size markers, positive and negative controls and/or instructions.

Hybridization conditions should be such that hybridization occurs only with the genes in the presence of other nucleic acid molecules. Under stringent hybridization conditions only highly complementary nucleic acid sequences hybridize. Preferably, such

conditions prevent hybridization of nucleic acids having 1 or 2 mismatches out of 20 contiguous nucleotides. Such conditions are defined supra.

The diseases for which detection of genes in a sample could be diagnostic include diseases in which nucleic acid (DNA and/or RNA) is amplified in comparison to normal cells. By "amplification" is meant increased numbers of DNA or RNA in a cell compared with normal cells.

The diseases that could be diagnosed by detection of nucleic acid in a sample preferably include central nervous system and metabolic diseases. The test samples suitable for nucleic acid probing methods of the present invention include, for example, cells or nucleic acid extracts of cells, or biological fluids. The samples used in the above-described methods will vary based on the assay format, the detection method and the nature of the tissues, cells or extracts to be assayed. Methods for preparing nucleic acid extracts of cells are well known in the art and can be readily adapted in order to obtain a sample that is compatible with the method utilized.

Alternatively, immunoassay kits can be provided which have containers container having antibodies specific for the nGPCR-x-protein and optionally, containers with positive and negative controls and/or instructions.

Kits may also be provided useful in the identification of GPCR binding partners such as natural ligands or modulators (agonists or antagonists). Substances useful for treatment of disorders or diseases preferably show positive results in one or more *in vitro* assays for an activity corresponding to treatment of the disease or disorder in question. Substances that modulate the activity of the polypeptides preferably include, but are not limited to, antisense oligonucleotides, agonists and antagonists, and inhibitors of protein kinases.

Methods of inducing immune response

Another aspect of the present invention is directed to methods of inducing an immune response in a mammal against a polypeptide of the invention by administering to the mammal an amount of the polypeptide sufficient to induce an immune response. The amount will be dependent on the animal species, size of the animal, and the like but can be determined by those skilled in the art.

Methods of identifying ligands

The invention also provides assays to identify compounds that bind nGPCR-x. One such assay comprises the steps of: (a) contacting a composition comprising a nGPCR-x with a compound suspected of binding nGPCR-x; and (b) measuring binding between the compound and nGPCR-x. In one variation, the composition comprises a cell expressing nGPCR-x on its surface. In another variation, isolated nGPCR-x or cell membranes comprising nGPCR-x are employed. The binding may be measured directly, *e.g.*, by using a labeled compound, or may be measured indirectly by several techniques, including measuring intracellular signaling of nGPCR-x induced by the compound (or measuring changes in the level of nGPCR-x signaling). Following steps (a) and (b), compounds identified as binding nGPCR-x may be tested in other assays including, but not limited to, *in vivo* models, to confirm or quantitate binding to nGPCR-x.

Specific binding molecules, including natural ligands and synthetic compounds, can be identified or developed using isolated or recombinant nGPCR-x products, nGPCR-x variants, or preferably, cells expressing such products. Binding partners are useful for purifying nGPCR-x products and detection or quantification of nGPCR-x products in fluid and tissue samples using known immunological procedures. Binding molecules are also manifestly useful in modulating (*i.e.*, blocking, inhibiting or stimulating) biological activities of nGPCR-x, especially those activities involved in signal transduction.

The DNA and amino acid sequence information provided by the present invention also makes possible identification of binding partner compounds with which a nGPCR-x polypeptide or polynucleotide will interact. Methods to identify binding partner compounds include solution assays, *in vitro* assays wherein nGPCR-x polypeptides are immobilized, and cell-based assays. Identification of binding partner compounds of nGPCR-x polypeptides provides candidates for therapeutic or prophylactic intervention in pathologies associated with nGPCR-x normal and aberrant biological activity.

The invention includes several assay systems for identifying nGPCR-x binding partners. In solution assays, methods of the invention comprise the steps of (a) contacting a nGPCR-x polypeptide with one or more candidate binding partner compounds and (b) identifying the compounds that bind to the nGPCR-x polypeptide. Identification of the compounds that bind the nGPCR-x polypeptide can be achieved by isolating the nGPCR-x polypeptide/binding partner complex, and separating the binding partner compound from

the nGPCR-x polypeptide. An additional step of characterizing the physical, biological, and/or biochemical properties of the binding partner compound is also comprehended in another embodiment of the invention, wherein compounds identified as binding nGPCR-x may be tested in other assays including, but not limited to, *in vivo* models, to confirm or quantitate binding to nGPCR-x. In one aspect, the nGPCR-x polypeptide/binding partner complex is isolated using an antibody immunospecific for either the nGPCR-x polypeptide or the candidate binding partner compound.

In still other embodiments, either the nGPCR-x polypeptide or the candidate binding partner compound comprises a label or tag that facilitates its isolation, and methods of the invention to identify binding partner compounds include a step of isolating the nGPCR-x polypeptide/binding partner complex through interaction with the label or tag. An exemplary tag of this type is a poly-histidine sequence, generally around six histidine residues, that permits isolation of a compound so labeled using nickel chelation. Other labels and tags, such as the FLAG® tag (Eastman Kodak, Rochester, NY), well known and routinely used in the art, are embraced by the invention.

In one variation of an *in vitro* assay, the invention provides a method comprising the steps of (a) contacting an immobilized nGPCR-x polypeptide with a candidate binding partner compound and (b) detecting binding of the candidate compound to the nGPCR-x polypeptide. In an alternative embodiment, the candidate binding partner compound is immobilized and binding of nGPCR-x is detected. Immobilization is accomplished using any of the methods well known in the art, including covalent bonding to a support, a bead, or a chromatographic resin, as well as non-covalent, high affinity interactions such as antibody binding, or use of streptavidin/biotin binding wherein the immobilized compound includes a biotin moiety. Detection of binding can be accomplished (i) using a radioactive label on the compound that is not immobilized, (ii) using of a fluorescent label on the non-immobilized compound, (iii) using an antibody immunospecific for the non-immobilized compound, (iv) using a label on the non-immobilized compound that excites a fluorescent support to which the immobilized compound is attached, as well as other techniques well known and routinely practiced in the art.

The invention also provides cell-based assays to identify binding partner compounds of a nGPCR-x polypeptide. In one embodiment, the invention provides a

method comprising the steps of contacting a nGPCR-x polypeptide expressed on the surface of a cell with a candidate binding partner compound and detecting binding of the candidate binding partner compound to the nGPCR-x polypeptide. In a preferred embodiment, the detection comprises detecting a calcium flux or other physiological event in the cell caused by the binding of the molecule.

Another aspect of the present invention is directed to methods of identifying compounds that bind to either nGPCR-x or nucleic acid molecules encoding nGPCR-x, comprising contacting nGPCR-x, or a nucleic acid molecule encoding the same, with a compound, and determining whether the compound binds nGPCR-x or a nucleic acid molecule encoding the same. Binding can be determined by binding assays which are well known to the skilled artisan, including, but not limited to, gel-shift assays, Western blots, radiolabeled competition assay, phage-based expression cloning, co-fractionation by chromatography, co-precipitation, cross linking, interaction trap/two-hybrid analysis, southwestern analysis, ELISA, and the like, which are described in, for example, *Current Protocols in Molecular Biology*, **1999**, John Wiley & Sons, NY, which is incorporated herein by reference in its entirety. The compounds to be screened include (which may include compounds which are suspected to bind nGPCR-x, or a nucleic acid molecule encoding the same), but are not limited to, extracellular, intracellular, biologic or chemical origin. The methods of the invention also embrace ligands, especially neuropeptides, that are attached to a label, such as a radiolabel (*e.g.*, ^{125}I, ^{35}S, ^{32}P, ^{33}P, ^{3}H), a fluorescence label, a chemiluminescent label, an enzymic label and an immunogenic label. Modulators falling within the scope of the invention include, but are not limited to, non-peptide molecules such as non-peptide mimetics, non-peptide allosteric effectors, and peptides. The nGPCR-x polypeptide or polynucleotide employed in such a test may either be free in solution, attached to a solid support, borne on a cell surface or located intracellularly or associated with a portion of a cell. One skilled in the art can, for example, measure the formation of complexes between nGPCR-x and the compound being tested. Alternatively, one skilled in the art can examine the diminution in complex formation between nGPCR-x and its substrate caused by the compound being tested.

In another embodiment of the invention, high throughput screening for compounds having suitable binding affinity to nGPCR-x is employed. Briefly, large numbers of

different test compounds are synthesized on a solid substrate. The peptide test compounds are contacted with nGPCR-x and washed. Bound nGPCR-x is then detected by methods well known in the art. Purified polypeptides of the invention can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the protein and immobilize it on the solid support.

Generally, an expressed nGPCR-x can be used for HTS binding assays in conjunction with its defined ligand, in this case the corresponding neuropeptide that activates it. The identified peptide is labeled with a suitable radioisotope, including, but not limited to, ^{125}I, ^{3}H, ^{35}S or ^{32}P, by methods that are well known to those skilled in the art. Alternatively, the peptides may be labeled by well-known methods with a suitable fluorescent derivative (Baindur *et al., Drug Dev. Res.*, **1994**, *33*, 373-398; Rogers, *Drug Discovery Today*, **1997**, *2*, 156-160). Radioactive ligand specifically bound to the receptor in membrane preparations made from the cell line expressing the recombinant protein can be detected in HTS assays in one of several standard ways, including filtration of the receptor-ligand complex to separate bound ligand from unbound ligand (Williams, *Med. Res. Rev.*, **1991**, *11*, 147-184; Sweetnam *et al., J. Natural Products*, **1993**, *56*, 441-455). Alternative methods include a scintillation proximity assay (SPA) or a FlashPlate format in which such separation is unnecessary (Nakayama, *Cur. Opinion Drug Disc. Dev.*, **1998**, *1*, 85-91 Bossé *et al., J. Biomolecular Screening*, **1998**, *3*, 285-292.). Binding of fluorescent ligands can be detected in various ways, including fluorescence energy transfer (FRET), direct spectrophotofluorometric analysis of bound ligand, or fluorescence polarization (Rogers, *Drug Discovery Today*, **1997**, *2*, 156-160; Hill, *Cur. Opinion* Drug *Disc. Dev.*, **1998**, *1*, 92-97).

Other assays may be used to identify specific ligands of a nGPCR-x receptor, including assays that identify ligands of the target protein through measuring direct binding of test ligands to the target protein, as well as assays that identify ligands of target proteins through affinity ultrafiltration with ion spray mass spectroscopy/HPLC methods or other physical and analytical methods. Alternatively, such binding interactions are evaluated indirectly using the yeast two-hybrid system described in Fields *et al.*, Nature, 340:245-246 (1989), and Fields *et al.*, Trends in Genetics, 10:286-292 (1994), both of

which are incorporated herein by reference. The two-hybrid system is a genetic assay for detecting interactions between two proteins or polypeptides. It can be used to identify proteins that bind to a known protein of interest, or to delineate domains or residues critical for an interaction. Variations on this methodology have been developed to clone genes that encode DNA binding proteins, to identify peptides that bind to a protein, and to screen for drugs. The two-hybrid system exploits the ability of a pair of interacting proteins to bring a transcription activation domain into close proximity with a DNA binding domain that binds to an upstream activation sequence (UAS) of a reporter gene, and is generally performed in yeast. The assay requires the construction of two hybrid genes encoding (1) a DNA-binding domain that is fused to a first protein and (2) an activation domain fused to a second protein. The DNA-binding domain targets the first hybrid protein to the UAS of the reporter gene; however, because most proteins lack an activation domain, this DNA-binding hybrid protein does not activate transcription of the reporter gene. The second hybrid protein, which contains the activation domain, cannot by itself activate expression of the reporter gene because it does not bind the UAS. However, when both hybrid proteins are present, the noncovalent interaction of the first and second proteins tethers the activation domain to the UAS, activating transcription of the reporter gene. For example, when the first protein is a GPCR gene product, or fragment thereof, that is known to interact with another protein or nucleic acid, this assay can be used to detect agents that interfere with the binding interaction. Expression of the reporter gene is monitored as different test agents are added to the system. The presence of an inhibitory agent results in lack of a reporter signal.

The yeast two-hybrid assay can also be used to identify proteins that bind to the gene product. In an assay to identify proteins that bind to a nGPCR-x receptor, or fragment thereof, a fusion polynucleotide encoding both a nGPCR-x receptor (or fragment) and a UAS binding domain (*i.e.*, a first protein) may be used. In addition, a large number of hybrid genes each encoding a different second protein fused to an activation domain are produced and screened in the assay. Typically, the second protein is encoded by one or more members of a total cDNA or genomic DNA fusion library, with each second protein-coding region being fused to the activation domain. This system is applicable to a wide variety of proteins, and it is not even necessary to know the identity

or function of the second binding protein. The system is highly sensitive and can detect interactions not revealed by other methods; even transient interactions may trigger transcription to produce a stable mRNA that can be repeatedly translated to yield the reporter protein.

Other assays may be used to search for agents that bind to the target protein. One such screening method to identify direct binding of test ligands to a target protein is described in U.S. Patent No. 5,585,277, incorporated herein by reference. This method relies on the principle that proteins generally exist as a mixture of folded and unfolded states, and continually alternate between the two states. When a test ligand binds to the folded form of a target protein (*i.e.*, when the test ligand is a ligand of the target protein), the target protein molecule bound by the ligand remains in its folded state. Thus, the folded target protein is present to a greater extent in the presence of a test ligand which binds the target protein, than in the absence of a ligand. Binding of the ligand to the target protein can be determined by any method that distinguishes between the folded and unfolded states of the target protein. The function of the target protein need not be known in order for this assay to be performed. Virtually any agent can be assessed by this method as a test ligand, including, but not limited to, metals, polypeptides, proteins, lipids, polysaccharides, polynucleotides and small organic molecules.

Another method for identifying ligands of a target protein is described in Wieboldt *et al.*, Anal. Chem., 69:1683-1691 (1997), incorporated herein by reference. This technique screens combinatorial libraries of 20-30 agents at a time in solution phase for binding to the target protein. Agents that bind to the target protein are separated from other library components by simple membrane washing. The specifically selected molecules that are retained on the filter are subsequently liberated from the target protein and analyzed by HPLC and pneumatically assisted electrospray (ion spray) ionization mass spectroscopy. This procedure selects library components with the greatest affinity for the target protein, and is particularly useful for small molecule libraries.

Other embodiments of the invention comprise using competitive screening assays in which neutralizing antibodies capable of binding a polypeptide of the invention specifically compete with a test compound for binding to the polypeptide. In this manner, the antibodies can be used to detect the presence of any peptide that shares one or more

antigenic determinants with nGPCR-x. Radiolabeled competitive binding studies are described in A.H. Lin *et al. Antimicrobial Agents and Chemotherapy*, **1997**, vol. 41, no. 10. pp. 2127-2131, the disclosure of which is incorporated herein by reference in its entirety.

As described above and in Example 5 below, the gene encoding nGPCR-74 (nucleic acid sequence SEQ ID NO:134, amino acid sequence SEQ ID NO:268) has been detected in brain tissue indicating that this nGPCR protein is a neuroreceptor. It is well known that other nGPCR-x are expressed in many different tissues, including the brain. Accordingly, natural binding partners of these molecules include neurotransmitters.

Identification of modulating agents

The invention also provides methods for identifying a modulator of binding between a nGPCR-x and a nGPCR-x binding partner, comprising the steps of: (a) contacting a nGPCR-x binding partner and a composition comprising a nGPCR-x in the presence and in the absence of a putative modulator compound; (b) detecting binding between the binding partner and the nGPCR-x; and (c) identifying a putative modulator compound or a modulator compound in view of decreased or increased binding between the binding partner and the nGPCR-x in the presence of the putative modulator, as compared to binding in the absence of the putative modulator. Following steps (a) and (b), compounds identified as modulating binding between nGPCR-x and a nGPCR-x binding partner may be tested in other assays including, but not limited to, *in vivo* models, to confirm or quantitate modulation of binding to nGPCR-x.

nGPCR-x binding partners that stimulate nGPCR-x activity are useful as agonists in disease states or conditions characterized by insufficient nGPCR-x signaling (*e.g.*, as a result of insufficient activity of a nGPCR-x ligand). nGPCR-x binding partners that block ligand-mediated nGPCR-x signaling are useful as nGPCR-x antagonists to treat disease states or conditions characterized by excessive nGPCR-x signaling. In addition nGPCR-x modulators in general, as well as nGPCR-x polynucleotides and polypeptides, are useful in diagnostic assays for such diseases or conditions.

In another aspect, the invention provides methods for treating a disease or abnormal condition by administering to a patient in need of such treatment a substance

that modulates the activity or expression of a polypeptide having sequences selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268.

Agents that modulate (*i.e.*, increase, decrease, or block) nGPCR-x activity or expression may be identified by incubating a putative modulator with a cell containing a nGPCR-x polypeptide or polynucleotide and determining the effect of the putative modulator on nGPCR-x activity or expression. The selectivity of a compound that modulates the activity of nGPCR-x can be evaluated by comparing its effects on nGPCR-x to its effect on other GPCR compounds. Following identification of compounds that modulate nGPCR-x activity or expression, such compounds may be further tested in other assays including, but not limited to, *in vivo* models, in order to confirm or quantitate their activity. Selective modulators may include, for example, antibodies and other proteins, peptides, or organic molecules that specifically bind to a nGPCR-x polypeptide or a nGPCR-x-encoding nucleic acid. Modulators of nGPCR-x activity will be therapeutically useful in treatment of diseases and physiological conditions in which normal or aberrant nGPCR-x activity is involved. nGPCR-x polynucleotides, polypeptides, and modulators may be used in the treatment of such diseases and conditions as infections, such as viral infections caused by HIV-1 or HIV-2; pain; cancers; metabolic and cardiovascular diseases and disorders (*e.g.*, type 2 diabetes, impaired glucose tolerance, dyslipidemia, obesity, anorexia, hypotension, hypertension, thrombosis, myocardial infarction, cardiomyopathies, atherosclerosis, *etc.*); Parkinson's disease; and psychotic and neurological disorders, including schizophrenia, migraine, ADHH, major depression, anxiety, mental disorder, manic depression, delirium, dementia, severe mental retardation and dyskinesias, such as Huntington's disease or Tourette's Syndrome, among others. nGPCR-x polynucleotides and polypeptides, as well as nGPCR-x modulators, may also be used in diagnostic assays for such diseases or conditions.

Methods of the invention to identify modulators include variations on any of the methods described above to identify binding partner compounds, the variations including techniques wherein a binding partner compound has been identified and the binding assay is carried out in the presence and absence of a candidate modulator. A modulator is identified in those instances where binding between the nGPCR-x polypeptide and the binding partner compound changes in the presence of the candidate modulator compared

to binding in the absence of the candidate modulator compound. A modulator that increases binding between the nGPCR-x polypeptide and the binding partner compound is described as an enhancer or activator, and a modulator that decreases binding between the nGPCR-x polypeptide and the binding partner compound is described as an inhibitor. Following identification of modulators, such compounds may be further tested in other assays including, but not limited to, *in vivo* models, in order to confirm or quantitate their activity as modulators.

The invention also comprehends high-throughput screening (HTS) assays to identify compounds that interact with or inhibit biological activity (*i.e.*, affect enzymatic activity, binding activity, *etc.*) of a nGPCR-x polypeptide. HTS assays permit screening of large numbers of compounds in an efficient manner. Cell-based HTS systems are contemplated to investigate nGPCR-x receptor-ligand interaction. HTS assays are designed to identify "hits" or "lead compounds" having the desired property, from which modifications can be designed to improve the desired property. Chemical modification of the "hit" or "lead compound" is often based on an identifiable structure/activity relationship between the "hit" and the nGPCR-x polypeptide.

Another aspect of the present invention is directed to methods of identifying compounds which modulate (*i.e.*, increase or decrease) an activity of nGPCR-x comprising contacting nGPCR-x with a compound, and determining whether the compound modifies activity of nGPCR-x. The activity in the presence of the test compared is measured to the activity in the absence of the test compound. Where the activity of the sample containing the test compound is higher than the activity in the sample lacking the test compound, the compound will have increased activity. Similarly, where the activity of the sample containing the test compound is lower than the activity in the sample lacking the test compound, the compound will have inhibited activity. Following the identification of compounds that modulate an activity of nGPCR-x, such compounds can be further tested in other assays including, but not limited to, *in vivo* models, in order to confirm or quantitate their activity.

The present invention is particularly useful for screening compounds by using nGPCR-x in any of a variety of drug screening techniques. The compounds to be screened include (which may include compounds which are suspected to modulate nGPCR-x

activity), but are not limited to, extracellular, intracellular, biologic or chemical origin. The nGPCR-x polypeptide employed in such a test may be in any form, preferably, free in solution, attached to a solid support, borne on a cell surface or located intracellularly. One skilled in the art can, for example, measure the formation of complexes between nGPCR-x and the compound being tested. Alternatively, one skilled in the art can examine the diminution in complex formation between nGPCR-x and its substrate caused by the compound being tested.

The activity of nGPCR-x polypeptides of the invention can be determined by, for example, examining the ability to bind or be activated by chemically synthesized peptide ligands. Alternatively, the activity of nGPCR-x polypeptides can be assayed by examining their ability to bind calcium ions, hormones, chemokines, neuropeptides, neurotransmitters, nucleotides, lipids, odorants, and photons. Alternatively, the activity of the nGPCR-x polypeptides can be determined by examining the activity of effector molecules including, but not limited to, adenylate cyclase, phospholipases and ion channels. Thus, modulators of nGPCR-x polypeptide activity may alter a GPCR receptor function, such as a binding property of a receptor or an activity such as G protein-mediated signal transduction or membrane localization. In various embodiments of the method, the assay may take the form of an ion flux assay, a yeast growth assay, a non-hydrolyzable GTP assay such as a [^{35}S]-GTP γS assay, a cAMP assay, an inositol triphosphate assay, a diacylglycerol assay, an Aequorin assay, a Luciferase assay, a FLIPR assay for intracellular Ca^{2+} concentration, a mitogenesis assay, a MAP Kinase activity assay, an arachidonic acid release assay (*e.g.*, using [^{3}H]-arachidonic acid), and an assay for extracellular acidification rates, as well as other binding or function-based assays of nGPCR-x activity that are generally known in the art. In several of these embodiments, the invention comprehends the inclusion of any of the G proteins known in the art, such as G_{16}, G_{15}, or chimeric G_{qd5} , G_{qs5}, G_{qo5}, G_{q25}, and the like. nGPCR-x activity can be determined by methodologies that are used to assay for FaRP activity, which is well known to those skilled in the art. Biological activities of nGPCR-x receptors according to the invention include, but are not limited to, the binding of a natural or an unnatural ligand, as well as any one of the functional activities of GPCRs known in the art. Non-limiting examples of GPCR activities include transmembrane signaling of various forms,

which may involve G protein association and/or the exertion of an influence over G protein binding of various guanidylate nucleotides; another exemplary activity of GPCRs is the binding of accessory proteins or polypeptides that differ from known G proteins.

The modulators of the invention exhibit a variety of chemical structures, which can be generally grouped into non-peptide mimetics of natural GPCR receptor ligands, peptide and non-peptide allosteric effectors of GPCR receptors, and peptides that may function as activators or inhibitors (competitive, uncompetitive and non-competitive) (*e.g.*, antibody products) of GPCR receptors. The invention does not restrict the sources for suitable modulators, which may be obtained from natural sources such as plant, animal or mineral extracts, or non-natural sources such as small molecule libraries, including the products of combinatorial chemical approaches to library construction, and peptide libraries. Examples of peptide modulators of GPCR receptors exhibit the following primary structures: GLGPRPLRFamide, GNSFLRFamide, GGPQGPLRFamide, GPSGPLRFamide, PDVDHVFLRFamide, and pyro-EDVDHVFLRFamide.

Other assays can be used to examine enzymatic activity including, but not limited to, photometric, radiometric, HPLC, electrochemical, and the like, which are described in, for example, *Enzyme Assays: A Practical Approach*, eds. R. Eisenthal and M. J. Danson, **1992**, Oxford University Press, which is incorporated herein by reference in its entirety.

The use of cDNAs encoding GPCRs in drug discovery programs is well-known; assays capable of testing thousands of unknown compounds per day in high-throughput screens (HTSs) are thoroughly documented. The literature is replete with examples of the use of radiolabeled ligands in HTS binding assays for drug discovery (see Williams, M*edicinal Research Reviews*, **1991**, *11*, 147-184.; Sweetnam, *et al.*, *J. Natural Products*, **1993**, *56*, 441-455 for review). Recombinant receptors are preferred for binding assay HTS because they allow for better specificity (higher relative purity), provide the ability to generate large amounts of receptor material, and can be used in a broad variety of formats (see Hodgson, *Bio/Technology*, **1992**, *10*, 973-980; each of which is incorporated herein by reference in its entirety).

A variety of heterologous systems is available for functional expression of recombinant receptors that are well known to those skilled in the art. Such systems include bacteria (Strosberg, *et al.*, *Trends in Pharmacological Sciences*, **1992**, *13*, 95-98),

yeast (Pausch, *Trends in Biotechnology*, **1997**, *15*, 487-494), several kinds of insect cells (Vanden Broeck, *Int. Rev. Cytology*, **1996**, *164*, 189-268), amphibian cells (Jayawickreme *et al.*, *Current Opinion in Biotechnology*, **1997**, *8*, 629-634) and several mammalian cell lines (CHO, HEK-293, COS, etc.; see Gerhardt, *et al.*, Eur. *J. Pharmacology*, **1997**, *334*, 1-23). These examples do not preclude the use of other possible cell expression systems, including cell lines obtained from nematodes (PCT application WO 98/37177).

In preferred embodiments of the invention, methods of screening for compounds that modulate nGPCR-x activity comprise contacting test compounds with nGPCR-x and assaying for the presence of a complex between the compound and nGPCR-x. In such assays, the ligand is typically labeled. After suitable incubation, free ligand is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular compound to bind to nGPCR-x.

It is well known that activation of heterologous receptors expressed in recombinant systems results in a variety of biological responses, which are mediated by G proteins expressed in the host cells. Occupation of a GPCR by an agonist results in exchange of bound GDP for GTP at a binding site on the G_α subunit; one can use a radioactive, non-hydrolyzable derivative of GTP, GTPγ[^{35}S], to measure binding of an agonist to the receptor (Sim *et al.*, Neuroreport, **1996**, *7*, 729-733). One can also use this binding to measure the ability of antagonists to bind to the receptor by decreasing binding of GTPγ[^{35}S] in the presence of a known agonist. One could therefore construct a HTS based on GTPγ[^{35}S] binding, though this is not the preferred method.

The G proteins required for functional expression of heterologous GPCRs can be native constituents of the host cell or can be introduced through well-known recombinant technology. The G proteins can be intact or chimeric. Often, a nearly universally competent G protein (e.g., $G_{\alpha 16}$) is used to couple any given receptor to a detectable response pathway. G protein activation results in the stimulation or inhibition of other native proteins, events that can be linked to a measurable response.

Examples of such biological responses include, but are not limited to, the following: the ability to survive in the absence of a limiting nutrient in specifically engineered yeast cells (Pausch, *Trends in Biotechnology*, **1997**, *15*, 487-494); changes in intracellular Ca^{2+} concentration as measured by fluorescent dyes (Murphy, *et al.*, *Cur.*

Opinion Drug Disc. Dev., **1998**, *1*, 192-199). Fluorescence changes can also be used to monitor ligand-induced changes in membrane potential or intracellular pH; an automated system suitable for HTS has been described for these purposes (Schroeder, *et al.*, *J. Biomolecular Screening*, **1996**, *1*, 75-80). Melanophores prepared from *Xenopus laevis* show a ligand-dependent change in pigment organization in response to heterologous GPCR activation; this response is adaptable to HTS formats (Jayawickreme *et al.*, *Cur. Opinion Biotechnology*, **1997**, *8*, 629-634). Assays are also available for the measurement of common second messengers, including cAMP, phosphoinositides and arachidonic acid, but these are not generally preferred for HTS.

Preferred methods of HTS employing these receptors include permanently transfected CHO cells, in which agonists and antagonists can be identified by the ability to specifically alter the binding of GTPγ[^{35}S] in membranes prepared from these cells. In another embodiment of the invention, permanently transfected CHO cells could be used for the preparation of membranes which contain significant amounts of the recombinant receptor proteins; these membrane preparations would then be used in receptor binding assays, employing the radiolabeled ligand specific for the particular receptor. Alternatively, a functional assay, such as fluorescent monitoring of ligand-induced changes in internal Ca^{2+} concentration or membrane potential in permanently transfected CHO cells containing each of these receptors individually or in combination would be preferred for HTS. Equally preferred would be an alternative type of mammalian cell, such as HEK-293 or COS cells, in similar formats. More preferred would be permanently transfected insect cell lines, such as *Drosophila* S2 cells. Even more preferred would be recombinant yeast cells expressing the *Drosophila melanogaster* receptors in HTS formats well known to those skilled in the art (*e.g.*, Pausch, *Trends in Biotechnology*, **1997**, *15*, 487-494).

The invention contemplates a multitude of assays to screen and identify inhibitors of ligand binding to nGPCR-x receptors. In one example, the nGPCR-x receptor is immobilized and interaction with a binding partner is assessed in the presence and absence of a candidate modulator such as an inhibitor compound. In another example, interaction between the nGPCR-x receptor and its binding partner is assessed in a solution assay, both in the presence and absence of a candidate inhibitor compound. In either assay, an

inhibitor is identified as a compound that decreases binding between the nGPCR-x receptor and its binding partner. Following the identification of compounds which inhibit ligand binding to nGPCR-x receptors, such compounds may be further tested in other assays including, but not limited to, *in vivo* models, in order to confirm or quantitate their activity. Another contemplated assay involves a variation of the dihybrid assay wherein an inhibitor of protein/protein interactions is identified by detection of a positive signal in a transformed or transfected host cell, as described in PCT publication number WO 95/20652, published August 3, 1995.

Candidate modulators contemplated by the invention include compounds selected from libraries of either potential activators or potential inhibitors. There are a number of different libraries used for the identification of small molecule modulators, including: (1) chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of random peptides, oligonucleotides or organic molecules. Chemical libraries consist of random chemical structures, some of which are analogs of known compounds or analogs of compounds that have been identified as "hits" or "leads" in other drug discovery screens, some of which are derived from natural products, and some of which arise from non-directed synthetic organic chemistry. Natural product libraries are collections of microorganisms, animals, plants, or marine organisms which are used to create mixtures for screening by: (1) fermentation and extraction of broths from soil, plant or marine microorganisms or (2) extraction of plants or marine organisms. Natural product libraries include polyketides, non-ribosomal peptides, and variants (non-naturally occurring) thereof. For a review, see Science 282:63-68 (1998). Combinatorial libraries are composed of large numbers of peptides, oligonucleotides, or organic compounds as a mixture. These libraries are relatively easy to prepare by traditional automated synthesis methods, PCR, cloning, or proprietary synthetic methods. Of particular interest are non-peptide combinatorial libraries. Still other libraries of interest include peptide, protein, peptidomimetic, multiparallel synthetic collection, recombinatorial, and polypeptide libraries. For a review of combinatorial chemistry and libraries created therefrom, see Myers, Curr. Opin. Biotechnol. 8:701-707 (1997). Identification of modulators through use of the various libraries described herein permits modification of the candidate "hit" (or "lead") to optimize the capacity of the "hit" to modulate activity.

Still other candidate inhibitors contemplated by the invention can be designed and include soluble forms of binding partners, as well as such binding partners as chimeric, or fusion, proteins. A "binding partner" as used herein broadly encompasses non-peptide modulators, as well as such peptide modulators as neuropeptides other than natural ligands, antibodies, antibody fragments, and modified compounds comprising antibody domains that are immunospecific for the expression product of the identified nGPCR-x gene.

The polypeptides of the invention are employed as a research tool for identification, characterization and purification of interacting, regulatory proteins. Appropriate labels are incorporated into the polypeptides of the invention by various methods known in the art and the polypeptides are used to capture interacting molecules. For example, molecules are incubated with the labeled polypeptides, washed to remove unbound polypeptides, and the polypeptide complex is quantified. Data obtained using different concentrations of polypeptide are used to calculate values for the number, affinity, and association of polypeptide with the protein complex.

Labeled polypeptides are also useful as reagents for the purification of molecules with which the polypeptide interacts including, but not limited to, inhibitors. In one embodiment of affinity purification, a polypeptide is covalently coupled to a chromatography column. Cells and their membranes are extracted, and various cellular subcomponents are passed over the column. Molecules bind to the column by virtue of their affinity to the polypeptide. The polypeptide-complex is recovered from the column, dissociated and the recovered molecule is subjected to protein sequencing. This amino acid sequence is then used to identify the captured molecule or to design degenerate oligonucleotides for cloning the corresponding gene from an appropriate cDNA library.

Alternatively, compounds may be identified which exhibit similar properties to the ligand for the nGPCR-x of the invention, but which are smaller and exhibit a longer half time than the endogenous ligand in a human or animal body. When an organic compound is designed, a molecule according to the invention is used as a "lead" compound. The design of mimetics to known pharmaceutically active compounds is a well-known approach in the development of pharmaceuticals based on such "lead" compounds. Mimetic design, synthesis and testing are generally used to avoid randomly screening a

large number of molecules for a target property. Furthermore, structural data deriving from the analysis of the deduced amino acid sequences encoded by the DNAs of the present invention are useful to design new drugs, more specific and therefore with a higher pharmacological potency.

Comparison of the protein sequence of the present invention with the sequences present in all the available databases showed a significant homology with the transmembrane portion of G protein coupled receptors. Accordingly, computer modeling can be used to develop a putative tertiary structure of the proteins of the invention based on the available information of the transmembrane domain of other proteins. Thus, novel ligands based on the predicted structure of nGPCR-x can be designed.

In a particular embodiment, the novel molecules identified by the screening methods according to the invention are low molecular weight organic molecules, in which case a composition or pharmaceutical composition can be prepared thereof for oral intake, such as in tablets. The compositions, or pharmaceutical compositions, comprising the nucleic acid molecules, vectors, polypeptides, antibodies and compounds identified by the screening methods described herein, can be prepared for any route of administration including, but not limited to, oral, intravenous, cutaneous, subcutaneous, nasal, intramuscular or intraperitoneal. The nature of the carrier or other ingredients will depend on the specific route of administration and particular embodiment of the invention to be administered. Examples of techniques and protocols that are useful in this context are, *inter alia*, found in Remington's Pharmaceutical Sciences, 16th edition, Osol, A (ed.), **1980**, which is incorporated herein by reference in its entirety.

The dosage of these low molecular weight compounds will depend on the disease state or condition to be treated and other clinical factors such as weight and condition of the human or animal and the route of administration of the compound. For treating human or animals, between approximately 0.5 mg/kg of body weight to 500 mg/kg of body weight of the compound can be administered. Therapy is typically administered at lower dosages and is continued until the desired therapeutic outcome is observed.

The present compounds and methods, including nucleic acid molecules, polypeptides, antibodies, compounds identified by the screening methods described herein, have a variety of pharmaceutical applications and may be used, for example, to

treat or prevent unregulated cellular growth, such as cancer cell and tumor growth. In a particular embodiment, the present molecules are used in gene therapy. For a review of gene therapy procedures, see *e.g.* Anderson, *Science*, **1992**, *256*, 808-813, which is incorporated herein by reference in its entirety.

The present invention also encompasses a method of agonizing (stimulating) or antagonizing a nGPCR-x natural binding partner associated activity in a mammal comprising administering to said mammal an agonist or antagonist to one of the above disclosed polypeptides in an amount sufficient to effect said agonism or antagonism. One embodiment of the present invention, then, is a method of treating diseases in a mammal with an agonist or antagonist of the protein of the present invention comprises administering the agonist or antagonist to a mammal in an amount sufficient to agonize or antagonize nGPCR-x-associated functions.

In an effort to discover novel treatments for diseases, biomedical researchers and chemists have designed, synthesized, and tested molecules that modulate the function of G protein coupled receptors. Some small organic molecules form a class of compounds that modulate the function of G protein coupled receptors.

Exemplary diseases and conditions amenable to treatment based on the present invention include, but are not limited to, thyroid disorders (*e.g.*, thyreotoxicosis, myxoedema); renal failure; inflammatory conditions (*e.g.*, Crohn's disease); diseases related to cell differentiation and homeostasis; rheumatoid arthritis; autoimmune disorders; movement disorders; CNS disorders (*e.g.*, pain including migraine; stroke; psychotic and neurological disorders, including anxiety, mental disorder, manic depression, anxiety, generalized anxiety disorder, post-traumatic-stress disorder, depression, bipolar disorder, delirium, dementia, severe mental retardation; dyskinesias, such as Huntington's disease or Tourette's Syndrome; attention disorders including ADD and ADHD, and degenerative disorders such as Parkinson's, Alzheimer's; movement disorders, including ataxias, supranuclear palsy, *etc.*); infections, such as viral infections caused by HIV-1 or HIV-2; metabolic and cardiovascular diseases and disorders (*e.g.*, type 2 diabetes, impaired glucose tolerance, dyslipidemia, obesity, anorexia, hypotension, hypertension, thrombosis, myocardial infarction, cardiomyopathies, atherosclerosis, *etc.*); proliferative diseases and cancers (*e.g.*, different cancers such as breast, colon, lung, *etc.*, and hyperproliferative

disorders such as psoriasis, prostate hyperplasia, *etc.*); hormonal disorders (*e.g.*, male/female hormonal replacement, polycystic ovarian syndrome, alopecia, *etc.*); sexual dysfunction, among others.

Methods of determining the dosages of compounds to be administered to a patient and modes of administering compounds to an organism are disclosed in U.S. Application Serial No. 08/702,282, filed August 23, 1996 and International patent publication number WO 96/22976, published August 1 1996, both of which are incorporated herein by reference in their entirety, including any drawings, figures or tables. Those skilled in the art will appreciate that such descriptions are applicable to the present invention and can be easily adapted to it.

The proper dosage depends on various factors such as the type of disease being treated, the particular composition being used and the size and physiological condition of the patient. Therapeutically effective doses for the compounds described herein can be estimated initially from cell culture and animal models. For example, a dose can be formulated in animal models to achieve a circulating concentration range that initially takes into account the IC_{50} as determined in cell culture assays. The animal model data can be used to more accurately determine useful doses in humans.

Plasma half-life and biodistribution of the drug and metabolites in the plasma, tumors and major organs can also be determined to facilitate the selection of drugs most appropriate to inhibit a disorder. Such measurements can be carried out. For example, HPLC analysis can be performed on the plasma of animals treated with the drug and the location of radiolabeled compounds can be determined using detection methods such as X-ray, CAT scan and MRI. Compounds that show potent inhibitory activity in the screening assays, but have poor pharmacokinetic characteristics, can be optimized by altering the chemical structure and retesting. In this regard, compounds displaying good pharmacokinetic characteristics can be used as a model.

Toxicity studies can also be carried out by measuring the blood cell composition. For example, toxicity studies can be carried out in a suitable animal model as follows: 1) the compound is administered to mice (an untreated control mouse should also be used); 2) blood samples are periodically obtained via the tail vein from one mouse in each treatment group; and 3) the samples are analyzed for red and white blood cell counts,

blood cell composition and the percent of lymphocytes versus polymorphonuclear cells. A comparison of results for each dosing regime with the controls indicates if toxicity is present.

At the termination of each toxicity study, further studies can be carried out by sacrificing the animals (preferably, in accordance with the American Veterinary Medical Association guidelines Report of the American Veterinary Medical Assoc. Panel on Euthanasia, Journal of American Veterinary Medical Assoc., 202:229-249, 1993). Representative animals from each treatment group can then be examined by gross necropsy for immediate evidence of metastasis, unusual illness or toxicity. Gross abnormalities in tissue are noted and tissues are examined histologically. Compounds causing a reduction in body weight or blood components are less preferred, as are compounds having an adverse effect on major organs. In general, the greater the adverse effect the less preferred the compound.

For the treatment of many diseases, the expected daily dose of a hydrophobic pharmaceutical agent is between 1 to 500 mg/day, preferably 1 to 250 mg/day, and most preferably 1 to 50 mg/day. Drugs can be delivered less frequently provided plasma levels of the active moiety are sufficient to maintain therapeutic effectiveness. Plasma levels should reflect the potency of the drug. Generally, the more potent the compound the lower the plasma levels necessary to achieve efficacy.

As discussed above, it is well known that GPCRs are expressed in many different tissues and regions, including in the brain. nGPCR-x mRNA transcripts may found in many other tissues, including, but not limited to peripheral blood lymphocytes, pancreas, ovary, uterus, testis, salivary gland, kidney, adrenal gland, liver, bone marrow, prostate, fetal liver, colon, muscle, and fetal brain, and may be found in many other tissues. Within the brain, nGPCR-x mRNA transcripts may be found in many tissues, including, but not limited to, frontal lobe, hypothalamus, pons, cerebellum, caudate nucleus, and medulla.

Sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134 will, as detailed above, enable screening the endogenous neurotransmitters/hormones/ligands which activate, agonize, or antagonize nGPCR-x and for compounds with potential utility in treating disorders including, but not limited to, thyroid disorders (*e.g.*, thyreotoxicosis, myxoedema); renal failure; inflammatory

conditions (*e.g.*, Crohn's disease); diseases related to cell differentiation and homeostasis; rheumatoid arthritis; autoimmune disorders; movement disorders; CNS disorders (*e.g.*, pain including schizophrenia, migraine; stroke; psychotic and neurological disorders, including anxiety, mental disorder, manic depression, anxiety, generalized anxiety disorder, post-traumatic-stress disorder, depression, bipolar disorder, delirium, dementia, severe mental retardation; dyskinesias, such as Huntington's disease or Tourette's Syndrome; attention disorders including ADD and ADHD, and degenerative disorders such as Parkinson's, Alzheimer's; movement disorders, including ataxias, supranuclear palsy, *etc.*); infections, such as viral infections caused by HIV-1 or HIV-2; metabolic and cardiovascular diseases and disorders (*e.g.*, type 2 diabetes, impaired glucose tolerance, dyslipidemia, obesity, anorexia, hypotension, hypertension, thrombosis, myocardial infarction, cardiomyopathies, atherosclerosis, *etc.*); proliferative diseases and cancers (*e.g.*, different cancers such as breast, colon, lung, *etc.*, and hyperproliferative disorders such as psoriasis, prostate hyperplasia, *etc.*); hormonal disorders (*e.g.*, male/female hormonal replacement, polycystic ovarian syndrome, alopecia, *etc.*); sexual dysfunction, among others.

For example, nGPCR-x may be useful in the treatment of respiratory ailments such as asthma, where T cells are implicated by the disease. Contraction of airway smooth muscle is stimulated by thrombin. Cicala *et al* (1999) Br J Pharmacol 126:478-484. Additionally, in bronchiolitis obliterans, it has been noted that activation of thrombin receptors may be deleterious. Hauck *et al.* (1999) Am J Physiol 277:L22-L29. Furthermore, mast cells have also been shown to have thrombin receptors. Cirino *et al* (1996) J Exp Med 183:821-827. nGPCR-x may also be useful in remodeling of airway structures in chronic pulmonary inflammation via stimulation of fibroblast procollagen synthesis. See, *e.g.*, Chambers *et al.* (1998) Biochem J 333:121-127; Trejo *et al.* (1996) J Biol Chem 271:21536-21541.

In another example, increased release of sCD40L and expression of CD40L by T cells after activation of thrombin receptors suggests that nGPCR-x may be useful in the treatment of unstable angina due to the role of T cells and inflammation. See Aukrust*et al.* (1999) Circulation 100:614-620.

A further example is the treatment of inflammatory diseases, such as psoriasis, inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis, and thyroiditis. Due to the tissue expression profile of nGPCR-x, inhibition of thrombin receptors may be beneficial for these diseases. See, *e.g.*, Morris *et al.* (1996) Ann Rheum Dis 55:841-843. In addition to T cells, NK cells and monocytes are also critical cell types which contribute to the pathogenesis of these diseases. See, *e.g.*, Naldini & Carney (1996) Cell Immunol 172:35-42; Hoffman & Cooper (1995) Blood Cells Mol Dis 21:156-167; Colotta *et al.* (1994) Am J Pathol 144:975-985.

Expression of nGPCR-x in bone marrow and spleen may suggest that it may play a role in the proliferation of hematopoietic progenitor cells. See DiCuccio *et al.* (1996) Exp Hematol 24:914-918.

As another example, nGPCR-x may be useful in the treatment of acute and/or traumatic brain injury. Astrocytes have been demonstrated to express thrombin receptors. Activation of thrombin receptors may be involved in astrogliosis following brain injury. Therefore, inhibition of receptor activity may be beneficial for limiting neuroinflammation. Scar formation mediated by astrocytes may also be limited by inhibiting thrombin receptors. See, *e.g*, Pindon *et al.* (1998) Eur J Biochem 255:766-774; Ubl & Reiser. (1997) Glia 21:361-369; Grabham & Cunningham (1995) J Neurochem 64:583-591.

nGPCR-x receptor activation may mediate neuronal and astrocyte apoptosis and prevention of neurite outgrowth. Inhibition would be beneficial in both chronic and acute brain injury. See, *e.g.*, Donovan *et al.* (1997) J Neurosci 17:5316-5326; Turgeon *et al* (1998) J Neurosci 18:6882-6891; Smith-Swintosky *et al.* (1997) J Neurochem 69:1890-1896; Gill *et al.* (1998) Brain Res 797:321-327; Suidan *et al.* (1996) Semin Thromb Hemost 22:125-133.

The attached Sequence Listing contains the sequences of the polynucleotides and polypeptides of the invention and is incorporated herein by reference in its entirety. As described above and in Example 5 below, the gene encoding nGPCR-74 (nucleic acid sequence SEQ ID NO:134, amino acid sequence SEQ ID NO:268) has been detected in brain tissue indicating that this nGPCR protein is a neuroreceptor. The identification of modulators such as agonists and antagonists is therefore useful for the identification of

compounds useful to treat neurological diseases and disorders. Such neurological diseases and disorders, including but are not limited to, schizophrenia, affective disorders, ADHD/ADD (*i.e.*, Attention Deficit-Hyperactivity Disorder/Attention Deficit Disorder), and neural disorders such as Alzheimer's disease, Parkinson's disease, migraine, and senile dementia as well as depression, anxiety, bipolar disease, epilepsy, neuritis, neurasthenia, neuropathy, neuroses, and the like.

Methods of Screening Human Subjects

Thus in yet another embodiment, the invention provides genetic screening procedures that entail analyzing a person's genome -- in particular their alleles for the nGPCR-x of the invention -- to determine whether the individual possesses a genetic characteristic found in other individuals that are considered to be afflicted with, or at risk for, developing a mental disorder or disease of the brain that is suspected of having a hereditary component. For example, in one embodiment, the invention provides a method for determining a potential for developing a disorder affecting the brain in a human subject comprising the steps of analyzing the coding sequence of one or more nGPCR-x genes from the human subject; and determining development potential for the disorder in said human subject from the analyzing step.

More particularly, the invention provides a method of screening a human subject to diagnose a disorder affecting the brain or genetic predisposition therefor, comprising the steps of: (a) assaying nucleic acid of a human subject to determine a presence or an absence of a mutation altering the amino acid sequence, expression, or biological activity of at least one seven transmembrane receptor that is expressed in the brain, wherein the seven transmembrane receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, or an allelic variant thereof, and wherein the nucleic acid corresponds to the gene encoding the seven transmembrane receptor; and (b) diagnosing the disorder or predisposition from the presence or absence of said mutation, wherein the presence of a mutation altering the amino acid sequence, expression, or biological activity of allele in the nucleic acid correlates with an increased risk of developing the disorder.

By "human subject" is meant any human being, human embryo, or human fetus. It will be apparent that methods of the present invention will be of particular interest to

individuals that have themselves been diagnosed with a disorder affecting the brain or have relatives that have been diagnosed with a disorder affecting the brain.

By "screening for an increased risk" is meant determination of whether a genetic variation exists in the human subject that correlates with a greater likelihood of developing a disorder affecting the brain than exists for the human population as a whole, or for a relevant racial or ethnic human sub-population to which the individual belongs. Both positive and negative determinations (i.e., determinations that a genetic predisposition marker is present or is absent) are intended to fall within the scope of screening methods of the invention. In preferred embodiments, the presence of a mutation altering the sequence or expression of at least one nGPCR-x seven transmembrane receptor allele in the nucleic acid is correlated with an increased risk of developing mental disorder, whereas the absence of such a mutation is reported as a negative determination.

The "assaying" step of the invention may involve any techniques available for analyzing nucleic acid to determine its characteristics, including but not limited to well-known techniques such as single-strand conformation polymorphism analysis (SSCP) [Orita *et al., Proc Natl. Acad. Sci. USA, 86*: 2766-2770 (1989)]; heteroduplex analysis [White *et al., Genomics, 12*: 301-306 (1992)]; denaturing gradient gel electrophoresis analysis [Fischer *et al., Proc. Natl. Acad. Sci. USA, 80*: 1579-1583 (1983); and Riesner *et al., Electrophoresis, 10*: 377-389 (1989)]; DNA sequencing; RNase cleavage [Myers *et al., Science, 230*: 1242-1246 (1985)]; chemical cleavage of mismatch techniques [Rowley *et al., Genomics, 30*: 574-582 (1995); and Roberts *et al., Nucl. Acids Res., 25*: 3377-3378 (1997)]; restriction fragment length polymorphism analysis; single nucleotide primer extension analysis [Shumaker *et al., Hum. Mutat., 7*: 346-354 (1996); and Pastinen *et al., Genome Res., 7*: 606-614 (1997)]; 5' nuclease assays [Pease *et al., Proc. Natl. Acad. Sci. USA, 91*:5022-5026 (1994)]; DNA Microchip analysis [Ramsay, G., *Nature Biotechnology, 16*: 40-48 (1999); and Chee *et al.*, U.S. Patent No. 5,837,832]; and ligase chain reaction [Whiteley *et al.*, U.S. Patent No. 5,521,065]. [See generally, Schafer and Hawkins, *Nature Biotechnology, 16*: 33-39 (1998).] All of the foregoing documents are hereby incorporated by reference in their entirety.

Thus, in one preferred embodiment involving screening nGPCR-x sequences, for example, the assaying step comprises at least one procedure selected from the group

consisting of: (a) determining a nucleotide sequence of at least one codon of at least one nGPCR-x allele of the human subject; (b) performing a hybridization assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences; (c) performing a polynucleotide migration assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences; and (d) performing a restriction endonuclease digestion to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences.

In a highly preferred embodiment, the assaying involves sequencing of nucleic acid to determine nucleotide sequence thereof, using any available sequencing technique. [See, *e.g.*, Sanger *et al., Proc. Natl. Acad. Sci. (USA), 74*: 5463-5467 (1977) (dideoxy chain termination method); Mirzabekov, *TIBTECH, 12*: 27-32 (1994) (sequencing by hybridization); Drmanac *et al., Nature Biotechnology, 16*: 54-58 (1998); U.S. Patent No. 5,202,231; and *Science, 260*: 1649-1652 (1993) (sequencing by hybridization); Kieleczawa *et al., Science, 258*: 1787-1791 (1992) (sequencing by primer walking); (Douglas *et al., Biotechniques, 14*: 824-828 (1993) (Direct sequencing of PCR products); and Akane *et al., Biotechniques 16*: 238-241 (1994); Maxam and Gilbert,*Meth. Enzymol., 65*: 499-560 (1977) (chemical termination sequencing), all incorporated herein by reference.] The analysis may entail sequencing of the entire nGPCR gene genomic DNA sequence, or portions thereof; or sequencing of the entire seven transmembrane receptor coding sequence or portions thereof. In some circumstances, the analysis may involve a determination of whether an individual possesses a particular allelic variant, in which case sequencing of only a small portion of nucleic acid -- enough to determine the sequence of a particular codon characterizing the allelic variant -- is sufficient. This approach is appropriate, for example, when assaying to determine whether one family member inherited the same allelic variant that has been previously characterized for another family member, or, more generally, whether a person's genome contains an allelic variant that has been previously characterized and correlated with a mental disorder having a heritable component.

In another highly preferred embodiment, the assaying step comprises performing a hybridization assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences. In a preferred embodiment, the hybridization involves a determination of whether nucleic acid derived from the human subject will hybridize with one or more oligonucleotides, wherein the oligonucleotides have nucleotide sequences that correspond identically to a portion of the nGPCR-x gene sequence taught herein, or that correspond identically except for one mismatch. The hybridization conditions are selected to differentiate between perfect sequence complementarity and imperfect matches differing by one or more bases. Such hybridization experiments thereby can provide single nucleotide polymorphism sequence information about the nucleic acid from the human subject, by virtue of knowing the sequences of the oligonucleotides used in the experiments.

Several of the techniques outlined above involve an analysis wherein one performs a polynucleotide migration assay, *e.g.*, on a polyacrylamide electrophoresis gel (or in a capillary electrophoresis system), under denaturing or non-denaturing conditions. Nucleic acid derived from the human subject is subjected to gel electrophoresis, usually adjacent to (or co-loaded with) one or more reference nucleic acids, such as reference GPCR-x encoding sequences having a coding sequence identical to all or a portion of SEQ ID NOS: 1 to 134 (or identical except for one known polymorphism). The nucleic acid from the human subject and the reference sequence(s) are subjected to similar chemical or enzymatic treatments and then electrophoresed under conditions whereby the polynucleotides will show a differential migration pattern, unless they contain identical sequences. [See generally Ausubel *et al.* (eds.), *Current Protocols in Molecular Biology*, New York: John Wiley & Sons, Inc. (1987-1999); and Sambrook *et al.*, (eds.), Molecular Cloning, *A Laboratory Manual*, Cold Spring Harbor, New York: Cold Spring Harbor Laboratory Press (1989), both incorporated herein by reference in their entirety.]

In the context of assaying, the term "nucleic acid of a human subject" is intended to include nucleic acid obtained directly from the human subject (*e.g.*, DNA or RNA obtained from a biological sample such as a blood, tissue, or other cell or fluid sample); and also nucleic acid derived from nucleic acid obtained directly from the human subject. By way of non-limiting examples, well known procedures exist for creating cDNA that is

complementary to RNA derived from a biological sample from a human subject, and for amplifying (*e.g.*, via polymerase chain reaction (PCR)) DNA or RNA derived from a biological sample obtained from a human subject. Any such derived polynucleotide which retains relevant nucleotide sequence information of the human subject's own DNA/RNA is intended to fall within the definition of "nucleic acid of a human subject" for the purposes of the present invention.

In the context of assaying, the term "mutation" includes addition, deletion, and/or substitution of one or more nucleotides in the GPCR gene sequence (*e.g.*, as compared to the seven transmembrane receptor-encoding sequences set forth of SEQ ID NO:1 to SEQ ID NO:134, and other polymorphisms that occur in introns (where introns exist) and that are identifiable via sequencing, restriction fragment length polymorphism, or other techniques. The various activity examples provided herein permit determination of whether a mutation modulates activity of the relevant receptor in the presence or absence of various test substances.

In a related embodiment, the invention provides methods of screening a person's genotype with respect to the nGPCR-x of the invention, and correlating such genotypes with diagnoses for disease or with predisposition for disease (for genetic counseling). For example, the invention provides a method of screening for an nGPCR-x hereditary mental disorder genotype in a human patient, comprising the steps of: (a) providing a biological sample comprising nucleic acid from the patient, the nucleic acid including sequences corresponding to said patient's nGPCR-x alleles; (b) analyzing the nucleic acid for the presence of a mutation or mutations; (c) determining a nGPCR-x genotype from the analyzing step; and (d) correlating the presence of a mutation in an nGPCR-x allele with a hereditary mental disorder genotype. In a preferred embodiment, the biological sample is a cell sample containing human cells that contain genomic DNA of the human subject. The analyzing can be performed analogously to the assaying described in preceding paragraphs. For example, the analyzing comprises sequencing a portion of the nucleic acid (*e.g.*, DNA or RNA), the portion comprising at least one codon of the nGPCR-x alleles.

Although more time consuming and expensive than methods involving nucleic acid analysis, the invention also may be practiced by assaying one or more proteins of a

human subject to determine the presence or absence of an amino acid sequence variation in GPCR protein from the human subject. Such protein analyses may be performed, *e.g.*, by fragmenting GPCR protein via chemical or enzymatic methods and sequencing the resultant peptides; or by Western analyses using an antibody having specificity for a particular allelic variant of the GPCR.

The invention also provides materials that are useful for performing methods of the invention. For example, the present invention provides oligonucleotides useful as probes in the many analyzing techniques described above. In general, such oligonucleotide probes comprise 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 nucleotides that have a sequence that is identical, or exactly complementary, to a portion of a human GPCR gene sequence taught herein (or allelic variant thereof), or that is identical or exactly complementary except for one nucleotide substitution. In a preferred embodiment, the oligonucleotides have a sequence that corresponds in the foregoing manner to a human GPCR coding sequence taught herein, and in particular, the coding sequences set forth in SEQ ID NO:1 to SEQ ID NO:134. In one variation, an oligonucleotide probe of the invention is purified and isolated. In another variation, the oligonucleotide probe is labeled, *e.g.*, with a radioisotope, chromophore, or fluorophore. In yet another variation, the probe is covalently attached to a solid support. [See generally Ausubel *et al.* and Sambrook *et al.*, *supra.*]

In a related embodiment, the invention provides kits comprising reagents that are useful for practicing methods of the invention. For example, the invention provides a kit for screening a human subject to diagnose a mental disorder or a genetic predisposition therefor, comprising, in association: (a) an oligonucleotide useful as a probe for identifying polymorphisms in a human nGPCR-x seven transmembrane receptor gene, the oligonucleotide comprising 6-50 nucleotides that have a sequence that is identical or exactly complementary to a portion of a human nGPCR-x gene sequence or nGPCR-x coding sequence, except for one sequence difference selected from the group consisting of a nucleotide addition, a nucleotide deletion, or nucleotide substitution; and (b) a media packaged with the oligonucleotide containing information identifying polymorphisms identifiable with the probe that correlate with mental disorder or a genetic predisposition

therefor. Exemplary information-containing media include printed paper package inserts or packaging labels; and magnetic and optical storage media that are readable by computers or machines used by practitioners who perform genetic screening and counseling services. The practitioner uses the information provided in the media to correlate the results of the analysis with the oligonucleotide with a diagnosis. In a preferred variation, the oligonucleotide is labeled.

In still another embodiment, the invention provides methods of identifying those allelic variants of GPCRs of the invention that correlate with mental disorders. For example, the invention provides a method of identifying a seven transmembrane allelic variant that correlates with a mental disorder, comprising steps of: (a) providing a biological sample comprising nucleic acid from a human patient diagnosed with a mental disorder, or from the patient's genetic progenitors or progeny; (b) analyzing the nucleic acid for the presence of a mutation or mutations in at least one seven transmembrane receptor that is expressed in the brain, wherein the at least one seven transmembrane receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134 or an allelic variant thereof, and wherein the nucleic acid includes sequence corresponding to the gene or genes encoding the at least one seven transmembrane receptor; (c) determining a genotype for the patient for the at least one seven transmembrane receptor from said analyzing step; and (d) identifying an allelic variant that correlates with the mental disorder from the determining step. To expedite this process, it may be desirable to perform linkage studies in the patients (and possibly their families) to correlate chromosomal markers with disease states. The chromosomal localization data provided herein facilitates identifying an involved nGPCR with a chromosomal marker.

The foregoing method can be performed to correlate the nGPCR-x of the invention to a number of disorders having hereditary components that are causative or that predispose persons to the disorder. For example, in one preferred variation, the disorder is a mental disorder.

Also contemplated as part of the invention are polynucleotides that comprise the allelic variant sequences identified by such methods, and polypeptides encoded by the allelic variant sequences, and oligonucleotide and oligopeptide fragments thereof that

embody the mutations that have been identified. Such materials are useful in*in vitro* cell-free and cell-based assays for identifying lead compounds and therapeutics for treatment of the disorders. For example, the variants are used in activity assays, binding assays, and assays to screen for activity modulators described herein. In one preferred embodiment, the invention provides a purified and isolated polynucleotide comprising a nucleotide sequence encoding a nGPCR-x receptor allelic variant identified according to the methods described above; and an oligonucleotide that comprises the sequences that differentiate the allelic variant from the nGPCR-x sequences set forth in SEQ ID NO:1 to SEQ ID NO:134. The invention also provides a vector comprising the polynucleotide (preferably an expression vector); and a host cell transformed or transfected with the polynucleotide or vector. The invention also provides an isolated cell line that is expressing the allelic variant nGPCR-x polypeptide; purified cell membranes from such cells; purified polypeptide; and synthetic peptides that embody the allelic variation amino acid sequence. In one particular embodiment, the invention provides a purified polynucleotide comprising a nucleotide sequence encoding a nGPCR-x seven transmembrane receptor protein of a human that is affected with a mental disorder; wherein said polynucleotide hybridizes to the complement of a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134 under the following hybridization conditions: (a) hybridization for 16 hours at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaC1, 10% dextran sulfate and (b) washing 2 times for 30 minutes at 60°C in a wash solution comprising 0.1x SSC and 1% SDS; and wherein the polynucleotide encodes a nGPCR-x amino acid sequence that differs from a sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, by at least one residue.

An exemplary assay for using the allelic variants is a method for identifying a modulator of nGPCR-x biological activity, comprising the steps of: (a) contacting a cell expressing the allelic variant in the presence and in the absence of a putative modulator compound; (b) measuring nGPCR-x biological activity in the cell; and (c) identifying a putative modulator compound in view of decreased or increased nGPCR-x biological activity in the presence versus absence of the putative modulator.

Additional features of the invention will be apparent from the following Examples. Examples 1, 2, and portions of Examples 3 and 5 are actual, while the remaining

Examples are prophetic. Additional features and variations of the invention will be apparent to those skilled in the art from the entirety of this application, including the detailed description, and all such features are intended as aspects of the invention. Likewise, features of the invention described herein can be re-combined into additional embodiments that also are intended as aspects of the invention, irrespective of whether the combination of features is specifically mentioned above as an aspect or embodiment of the invention. Also, only such limitations which are described herein as critical to the invention should be viewed as such; variations of the invention lacking limitations which have not been described herein as critical are intended as aspects of the invention.

EXAMPLES

EXAMPLE 1: IDENTIFICATION OF nGPCR-X

A. Database search

The Celera database was searched using known GPCR receptors as query sequences to find patterns suggestive of novel G protein-coupled receptors. Positive hits were further analyzed with the GCG program BLAST to determine which ones were the most likely candidates to encode G protein-coupled receptors, using the standard (default) alignment produced by BLAST as a guide.

Briefly, the BLAST algorithm, which stands for Basic Local Alignment Search Tool is suitable for determining sequence similarity (Altschul *et al.*, J. Mol. Biol., 1990, 215, 403-410, which is incorporated herein by reference in its entirety). Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/). This algorithm involves first identifying high scoring sequence pair (HSPs) by identifying short words of length W in the query sequence that either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al.*, *supra*). These initial neighborhood word hits act as seeds for initiating searches to find HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Extension for the word hits in each direction are halted when: 1) the cumulative alignment score falls off by the quantity X

from its maximum achieved value; 2) the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or 3) the end of either sequence is reached. The Blast algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The Blast program uses as defaults a word length (W) of 11, the BLOSUM62 scoring matrix (see Henikoff et al., Proc. Natl. Acad. Sci. USA, 1992, 89, 10915-10919, which is incorporated herein by reference in its entirety) alignments (B) of 50, expectation (E) of 10, M=5, N=4, and a comparison of both strands.

The BLAST algorithm (Karlin *et al.*, Proc. Natl. Acad. Sci. USA, 1993, 90, 5873-5787, which is incorporated herein by reference in its entirety) and Gapped BLAST perform a statistical analysis of the similarity between two sequences. One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a nucleic acid is considered similar to a GPCR gene or cDNA if the smallest sum probability in comparison of the test nucleic acid to a GPCR nucleic acid is less than about 1, preferably less than about 0.1, more preferably less than about 0.01, and most preferably less than about 0.001.

Homology searches are performed with the program BLAST version 2.08. A collection of 340 query amino acid sequences derived from GPCRs was used to search the genomic DNA sequence using TBLASTN and alignments with an E-value lower than 0.01 were collected from each BLAST search. The amino acid sequences have been edited to remove regions in the sequence that produce non-significant alignments with proteins that are not related to GPCRs.

Multiple query sequences may have a significant alignment to the same genomic region, although each alignment may not cover exactly the same DNA region. A procedure is used to determine the region of maximum common overlap between the alignments from several query sequences. This region is called the consensus DNA region. The procedure for determining this consensus involves the automatic parsing of the BLAST output files using the program MSPcrunch to produce a tabular report. From this tabular report the start and end of each alignment in the genomic DNA is extracted. This information is used by a PERL script to derive the maximum common overlap. These regions are reported in the form of a unique sequence identifier, a start and the end

position in the sequence. The sequences defined by these regions were extracted from the original genomic sequence file using the program fetchdb.

The consensus regions are assembled into a non-redundant set by using the program phrap. After assembly with phrap a set of contigs and singletons were defined as candidate DNA regions coding for nGPCRs. These sequences were then submitted for further sequence analysis.

Further sequence analysis involves the removal of sequences previously isolated and removal of sequences that are related to olfactory GPCR's.

nGPRCR-x cDNAs were sequenced directly using an ABI377 fluorescence-based sequencer (Perkin-Elmer/Applied Biosystems Division, PE/ABD, Foster City, CA) and the ABI PRISM™ Ready Dye-Deoxy Terminator kit with Taq FS™ polymerase. Each ABI cycle sequencing reaction contained about 0.5 μg of plasmid DNA. Cycle-sequencing was performed using an initial denaturation at 98°C for 1 minute, followed by 50 cycles using the following parameters: 98°C for 30 seconds, annealing at 50°C for 30 seconds, and extension at 60°C for 4 minutes. Temperature cycles and times were controlled by a Perkin-Elmer 9600 thermocycler. Extension products were purified using Centriflex™ gel filtration cartridges (Advanced Genetic Technologies Corp., Gaithersburg, MD). Each reaction product was loaded by pipette onto the column, which is then centrifuged in a swinging bucket centrifuge (Sorvall model RT6000B tabletop centrifuge) at 1500 x *g* for 4 minutes at room temperature. Column-purified samples were dried under vacuum for about 40 minutes and then dissolved in 5μl of a DNA loading solution (83% deionized formamide, 8.3mM EDTA, and 1.6 mg/ml Blue Dextran). The samples were then heated to 90°C for three minutes and loaded into the gel sample wells for sequence analysis using the ABI377 sequencer. Sequence analysis was performed by importing ABI377 files into the Sequencer program (Gene Codes, Ann Arbor, MI). Generally, sequence reads of 700 bp were obtained. Potential sequencing errors were minimized by obtaining sequence information from both DNA strands and by re-sequencing difficult areas using primers annealing at different locations until all sequencing ambiguities were removed.

The following Table 5 contains the sequences of the polynucleotides and polypeptides of the invention. The transmembrane domains within the polypeptide sequence are identified by underlining.

TABLE 5
The following DNA sequence Seq-2356 <SEQ ID NO. 1> was identified in *H. sapiens*: GGAATTTAGTTGGGCAGAAGGGGAATAAAGTGAGGATGGTTAATGGGTACAAAAAATAGT TAGGAAAAAAATGAATAAGATCTAGTATTAGATAGCACAACAGGGTGATTGTAGTCAATA TAATTTAGTTGTACAATTTAAAATAACTAAAAGAATATAACTGGATTGTTTGTAACACAA ATGATAAACGCTTGAGGTAATGGATACGATATTTACCCTGATGTAATTATTACACATTGC ACGTCTGTATTCAAAATACCCCATCTAACTCATAAATATTTATATCTACTATCTACACAA AAAATTAAAAATTAAAAAAATTTTTGCATGATGATCTTAACTGAATTTTTCAATAATAAA ACATTGTCTGTTTTCATTAAGTTCAATTTAGCAATTTCAATTATGTTTAATTATTTTTGC ATCCTGAATAAAAAATCTTCTTATACTGCAAGATTTTGAAGGCAATCTAGACTTACTTCT AGAATTGTTATGTTCTACCTGTTATAATCAGGCTTACAATTCATGTCCAATTAATTTTCA TATGTAAAGTGAGTTATATTTTTCATGAAGTTGTTCAGTTTTTCAGCCCCACTTAAAAAA ATGTAGAATTGTTTCTTGCTCAGTTAAACTGACCTGCTTTTT The following amino acid sequence <SEQ ID NO. 135> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 1: KKQVSLTEQETILHFFKWGKTEQLHEKYNSLYIKLIGHELALQVEHNNSRSKSRLPSKSCSIRRFFIQDAK IIKHNNCIELNENRQCFIIEKFSDHHAKIFLIFNFLCRIIFMSMGYFEYRRAMCNNYIRVNIVSITSSVYH LCYKQSSYILLVILNCTTKLYLQSPCCAIYILFIFFLTIFCTHPSSLYSPSAQLNS
The following DNA sequence Seq-2357 SEQ ID NO. 2> was identified in *H. sapiens*: CAGGTGCAGCATCGTGTCCTCAGTGTCCTGCCCCCTGCTTCCACCCGGTGTCGACAGCTG CACGGTCCACCCCACGCCTGCCTTTCCATCGTTCCTCATCAGCCCTGTGATCTTTCCTGT GGCCCTGCTGTGCTGGTGCCCTGTGAGGTCCTGTGGACACAAGAGACTGCACGGGCCACA CCCCCAGCTGGGTGAGTCCTCTCCCTCCTGGGTACTCTGGACAGTAAAGAAAGATGGACA CGTGGGCTCCGTGGAGCATGAGGTAGTCCAGGACCTCGGCGGCCACAGGTCCTGCCTCCC TGCTTCTCGTGCCCTCCCTCCCTTTGGGTCTCTGCTCCACCTCGGTAAACGCTTCGTTCC CACCCCTCGAAGGGTAAATCGAGCTCCTTGGTGGTAAAGCACCCACTGCCCCTAGTCAGA GGGTCCCTCCTCTCTGATGTCATGGTGCCCTGGTCTGCCTGGTAGAATTTTAGCTGCTTT ATAACCTGGTCCTGAAATGAACCACTGGGAAGAAATAGGGTAAAATGAACACACAGCTGC CACACTGCATCCCAACCCTGTGTGACCCTATCACCGCAGACTTTTGTGGCAAGATGACAG CATCTCAGTTTGCTTGAGAAGCTTATTTTTGCCAAGGCTGTTACCACCAGGCAGGCACCA The following amino acid sequence <SEQ ID NO. 136> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 2: RCSIVSSVSCPLLPPGVDSCTVHPT<u>PAFPSFLISPVIFPVALLCWCPV</u>RSCGHKRLHGPHPQLGESSPSWV LWTVKKDGHVGSVEHEVVQDLGGHRSCLPASRALPPFGSLLHLGKRFVPTPRRVNRAPWWSTHCPSEGPSS LMSWCPGLPGRILAALPGPEMNHWEEIGNEHTAATLHPNPVPYHRRLLWQDDSISVCLRSLFLPRLLPPGR H
The following DNA sequence Seq-2358 <SEQ ID NO. 3> was identified in *H. sapiens*:

CTATTATTTCTTAACATACTGCATTTTTCCGATTCTCTCTAAGTATCTGTTTCTGTAACT
CCTATTGGACATTTACTTCTCTTTCACATTGTCTGCTTTATCTCTTAACTTTTGTGTTTT
CTGTCTCTCACTGCTGTATTGTGAGTTATTACTTAGCTCTTCCAGTTAATTCTTTAAGCT
TTTTTTGTAATCTCTTTATCAGTTCATTGTGTTTATTATTTCAGTGACTAAATTTAATTG
CTCAAAGTTTTATTTGGTCGTTTAAAATTTGCTTTTGTCTTCATAGTTATTTTGTCCTGT
TCTCTTTATCTCTTTATTTATTTTTGATGCTTTCATCTGCTTATTATTTTTAAGATATTT
ATTTCTTAGCCTCTTTGAGATATTCTATTATCTCTGGTCCTAGGATCATTAAATCTCCCA
CTACGTCTGTAGACTC

The following amino acid sequence <SEQ ID NO. 137> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 3:

IISHTAFFRFSLSICFCNSYWTFTSLSHCLLYLLTFVFSVSHCCIVSYYLALPVNSLSFFCNLFISSLCLL
FQLNLIAQSFIWSFKICFCLHSYFVLFSLSLYLFLMLSSAYYFDIYFLASLRYSIISGPRIIKSPTTSVD

The following DNA sequence Seq-2359 <SEQ ID NO. 4> was identified in *H. sapiens*:

ACTTCTGGGCCACGGAAAGCCCTACTGTCTAAATGCTTTTCAGGCCAATTTGAAGAAGTA
ATTAGACTTACTGGAAGCTTCTGTGAATAATTCTGCAAGTACAATTATGGACTTCCCAGG
AAATATTGCCTTCAATATAGAAAAGCTTGTCAGTTGATTCTGATGAGATATATGTAAAAT
TTGAGATTTTGATATTAGAATGAGTAAAATGATGACATCACGATGTATTAAAGTTGGGGT
TTATTTTTTGGAATTAATTGTCATCAGGTAAAAAGCCAGCTATAAGTCAAATAAAATATA
ATCATGTTCTTCCGTCTTTAGCACTCATCTTTTCTTGTTCTAAATGTTGACAAATGACTG
TAAATTTAACAAGCTTATAGATAATAATTGAAAAGTCTTCTAAGAACTGAAAATTGATAA
ACACATGGCAATGGCAGGCTATTGCAGTGCAATTATAAGATGTTGTGTGGATGCCCCTGA
AGTGCCTATAAATGAATGTGACTTCAGTACTACTGCCAAATGAGTCCAATATCCCACAAA
TGAACTGAAAATAAAGTGCCTGGAATACTGTGTCTACAGTGTCACTGTAAAGTTACTGTC
ATGCTGTATTACTGAAATGATTTGCTGGAAAGTAACATGGCACATATATGCACCAAGAGA
GTTAAATCTCATCTTATTCTATGAAAAATCATGTTAACCATTCATGA

The following amino acid sequence <SEQ ID NO. 138> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 4:

HEWLTFFIEDEILSWCIYVPCYFPANHFSNTAQLYSDTVDTVFQALYFQFICGILDSFGSSTEVTFIYRHF
RGIHTTSYNCTAIACHCHVFINFQFLEDFSIIIYKLVKFTVICQHLEQEKMSAKDGRTLYFILIAGFLPDD
NFQKINPNFNTSCHHFTHSNIKISNFTYISSESTDKLFYIEGNISWEVHNCTCRIIHRSFQVLLLQIGLKS
ITVGLSVAQK

The following DNA sequence Seq-2360 <SEQ ID NO. 5> was identified in *H. sapiens*:

AACATTATTACTTTCTTTTATGAATATTCTTGGTCTTTCCAAAACAAAACAAGCTATTGG
TTTAATAAATTATGGTATAATCAAATAATGAAACTCTATGCATTTGTTAAAGTAACTTTT
CAAAAGAATATCTTGTAACATAGAATAACAGATCCTAGTGCATTACCCACTCTTTGGGCT
TTATCGCTTTTCCACCATCATTATCTGCATCACTGCCTGCAGGTTTTCTACACGGCCAGG
GTTGGTCTCTGCCTGCTCAATAGTCAAGTCAAAAGAGGCAGGAAATTAACACCCTCTGGA
GGCAGCCTTTGAGGAATGATCCATGGGAGGTGGAGTATAAATACCTCAGCTCTGTTTCCT
CTAGAGATATAACTAAGGAATGGGTTTTACATTGTTTCTCAGAGTTTCCTCAAGGTTTTA
AACTTCAATCACCCACAGGGGGTAGTGGGCTTTATCATAGTATACATCCCTTTGTGGCTT
CCCTTCCTTCTTGTCTCACTTCTCCATTCCAAACTAGGATTTATTTCTT

The following amino acid sequence <SEQ ID NO. 139> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 5:

NIITFFYEYSWSFQNKTSYWFNKLWYNQIMKLYAFVKVTFQKNILHRITDPSALPTLWALSLFHHHYLHHC
LQVFYTARVGLCLLNSQVKRGRKLTPSGGSLGMIHGRWSINTSALFPLEILRNGFYIVSQSFLKVLNFNHP
QGVVGFIIVYIPLWLPFLLVSLLHSKLGFIS

The following DNA sequence Seq-2361 <SEQ ID NO. 6> was identified in *H. sapiens*:

AAGTATTCTTGTCACGGAAAGAAGAAAAGGGTTGGGTAGTTACAGGGGGACAACAATGCC
AGAACTGGGGAGTGTGGACTGGGATACAAGAGAATGAGGGAGCTCAGGATGAGCAGAAGG
GCGGGGAAGCAATATTCATTAAGCACCTTCTATGTGCCAGTCAATAGGCCAGGCTTCAAA
TTATTACCTTGCTGAAATCTTCACAGCAGCCCTCTAATAGGTATTTATCCCTGATTCCAT
ATCCATGCTCTGCTTCCCCTCCTATTACAATGGCTGAAGAATTCAAACCCCTTTCAAAGG
CTAGCACTGTCATTTGTCCTCTAGATCCCATCCCCTCCATTTTTCTTTTTATTGAAACAT
TCTCAATGGTATTCAAACATACTCTGCTCTCTCTTCTATTAAATAGGCAAATGCAACTCA
TCAAGCTCTTTTTCTCCCTTGGCTACTGCCCCATTTCTCTACTTCCTTTCATGGCAGAAC
TTCTCGAAAGAGTTTTTCACAATCACTTCATTTCCACACCTCTAACTGACTTTTGAACAC
AACTAGAGGAGGAGTAGGAGGGGACACTCATTCCAAAGTGTCCAATTAAGCCCAATCCTT
TAAAAGTATTATGTTGTCATGATGGCTGTTAAGAGCATGGTGAAAAGATATTAGAATAAG
ATGTGGGGAATCATGACCGTGAGACAGA

The following amino acid sequence <SEQ ID NO. 140> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 6:

VFLSRKEEKGWVVTGGQQCQNWGVWTGIQENEGAQDEQKGGEAIFIKHLLCASQARLQIITLLKSSQQPSN
RYLSLIPYPCSASPPITMAEEFKPLSKASTVICPLDPIPSIFLFIETFSMVFKHTLLSLLLNRQMQLIKLF
FSLGYCPISLLPFMAELLERVFHNHFISTPLTDFTQLEEEEGTLIPKCPIKPNPLKVLCCHDGCEHGEKIL
EDVGNHDRET

The following DNA sequence Seq-2362 <SEQ ID NO. 7> was identified in *H. sapiens*:

AAAGAAAAAGAAAGAGTAGTGTAACAATTCCACTTCTGGATTAACATTGTAAGGAGACTG
TGGACCTGTTACAGCAGAAAACAGATATAATAGGCAAAAATTATTTTTTAAAAAATCTCC
AGAAATTGTTCTAAAAACATACAGCAGACTTTTAAAAAACTTGTCTGAGAAAATGTACTA
AATCTCTGTAAGACAAACAAGAGTCTGTGGCACGTGAGCAATGTTTGCCTCACTCTAACC
TCTCCCTCCCAGGTCACCTTCATAAAAGTTCAACTCTGGGAAGGTGTGCCCAAATTGAGA
TTACCTGCCCCATTAATTTCCAATCAAAGGATACAGTATATCACCAGGAAGGTAGCCACC
AGCATTTCTCAGCCCCTCTTACTCCAAGTTGCAGAGGATAAATTCCTGGTGAGTATGGCC
AGGAGGCCACGTGGCCACCTGGCCACCACTAATAGATCAGAGGATTAATCTCACACATGG
AAGGATGAGCATACTGGGCCCCTGATTGCCCTGACCCCAGCTTACTTATAGGATGGAAGT
TTCACATCAGGA

The following amino acid sequence <SEQ ID NO. 141> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 7:

SCETSILVSWGQGNQGPSMLILPCVRLILSISGGQVATWPPGHTHQEFILCNLEEGLRNAGGYLPGDILYP
LIGNWGRSQFGHTFPELNFYEGDLGGRGSEANIAHVPQTLVCLTEIYIFSDKFFKSLLYVFRTISGDFLKN
NFCLLYLFSAVTGPQSPYNVNPEVELLHYSFFFF

The following DNA sequence Seq-2363 <SEQ ID NO. 8> was identified in *H. sapiens*:

AGTTAACAAAAAAATACTACTTAACCTCTGCTAGAACATAATGTGATACATTTTTGACAC
CTCTTAGCTTCTTTAGCTGAATTTCAGAAATGCAACCATTAGTATTAAGAAGCAGGTACT
AAGGATTTTCCAAATCATTTTGTTATTCTTATCAATATTTCTAGTATTCTTTTAGATCCC

TTCACTCACTTTCTCTATTGCTTTCCATTTCCTGAAGTTTAAATAAAATTTCCCTTCTG
TTTGTCTTGTAGGAAAAATCATCATGCTTACCACATAGAATGTGAGTTGTAGGAGAGACA
CAATGGGAGACATCGGTTAAGGGACAAAAGACATTAACATTTTAGGTGATTGTGAGTTCA
TAATTTTTCCAGAACACAAGCATTGCATGGCTACTCTAATATACTAGATTATTAAAATAG
ATATATCTTTGCCCTACCTGATAAACACTATTTGTATAAGTGAATATATTTTTAATATTA
ATCCAATATATTTCATAAGAAATATTTGATTTGCAAAGTAATCTGAGCATTACGATGATT
CCCTATCTAAATACTGGCATGGTGAAAATGAGGACAAATCTACCCTTTCTCTAATGTAGT
TACAGGCAAGCTATACTCATATAATAAACATAGAACGTACAATCAAAACCAATGCATGAG
TGTAGGATGCAACTAAAGTCAAGA

The following amino acid sequence <SEQ ID NO. 142> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 8:

SQKNTTPLLEHNVIHFHLLASLAEFQKCNHYEAGTKDFPNHFVILINISSILLDPFTHFLYCFPFPEVLNK
ISLLFVLEKSSCLPHRMVVGETQWETSVKGQKTLTFVIVSSFFQNTSIAWLLYTRLLKIYLCPTTLFVVNI
FLILIQYISEIFDLQSNLSITMIPYLNTGMVKMRTNLPFLCSYRQAILITNVQSKPMHECRMQLKSR

The following DNA sequence Seq-2364 <SEQ ID NO. 9> was identified in *H. sapiens*:

ATCATTTTGATAACCAGTCTGATCTGAGAAAATTAAACCATGTCATTCAAAACATGTCCT
CCCCAAATTTAAGAAACATTAGGTCAATCTCCTGGTTAAATAATAGCTGTATGTTTTAGT
AGATTTTGAAATATTATGTAATCATTTGAAATTATAAGCTTCTGGCCCACAACTTGACTG
ACAAATACCTGTTTCATTATTTTTAACTAGCCTTTGTTGGACTACATATCTCCAAAGACA
AAAGAAAGATAAAAGTTGAAATAATCCAACAGTTATCCTACACAAAAGTATGACAAAATT
ACCGTTGCAGAAATTGAACTCATCAAGCCTGAACTTTTGACTTTGAACAATTACATGGAA
GAGTGCCACCATGGTGAACTGTCAGACCTGTACAGCATCACAGCCAACTCTATACACAAA
CAAGGGTGGGCTGTATTCTGACCATTATTGGAATAAATTATCCTGATTACCTAATGTCTC
TTCACACCCACTAAATTATTTATTATTATTATATTTTACACTGCCATCAAATTAAAGTT
GCTAAAACACAACTTTGCTCATGTTCAAAATTTCTATAGTGTGCCTCAACAATCACTAAC
TAATCCTCAGAATTAATTACCTACTAATTTGTTTTTGACAT

The following amino acid sequence <SEQ ID NO. 143> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 9:

SFPVSEKIKPCHSKHVLPKFKKHVNLLVKLYVLVDFEILCNHLKLASGPQLDQIPVSLFLTSLCWTTYLQR
QKKDKSNNPTVILHKSMTKLPLQKLNSSSLNFLTITWKSATMVNCQTCTASQPTLYTNKGGLYSDHYWNKL
SLPNVSSHPLNYLLLLYFYTAIKLKLLKHNFAHVQNFYSVPQQSLTNPQNLPTNLFLT

The following DNA sequence Seq-2365 <SEQ ID NO. 10> was identified in *H. sapiens*:

TCTAGAATCTATACATACTATGTCCAATCCCTGTTCCACAAGTAGTTATTTATATGTGCG
AAGGTTCATACTCCTGATTTTCCTTTTGCTCCAGGGCAAAGAAAAGATACTGAAATACAA
GGTGAGCTTATATCAGCCCAGTAGTAAGCCAGTGAGGGCTACCACAGTTTGGAAGAAGCA
GGGTGAAACTTTTACATGAGATTGGGGGGAAAAACCATACTGAATAATAAAGGGTTTTAA
CTGAGATTGAAAGATAGTGCTTTGAGAAGCACACAAAAGATTCAAAATGGGCGTATAAAG
AATGACCTGTGCTGAAAAACACATTTTTGCGCTACAAGGGACCCAATTGACTAGATGAGA
ATTTGTGTGGAAAAGGAGTTGATAAGGCAGGCTGGCACATTGCAGCCAATCTGTGAAAGG
CTTTTCATGTCCTGTGAACAGGAAATCACATATCACAAGAGTGGTCTAGGAATCTGTGTC
TGGCAACCCTACAGTGGGGCAGACTGAAGAGGGAATAACG

The following amino acid sequence <SEQ ID NO. 144> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 10:

VIPSSVCPTVGLPDTDSTTLVICDFLFTGHEKPFTDWLQCASLPYQLLFHTNSHLVNWVPCSAKMCFSAQV
ILYTPILNLLCASQSTIFQSQLKPFIIQYGFSPQSHVKVSPCFFQTVVALTGLLLGYKLTLYFSIFSLPWS
KRKIRSMNLRTYKLLVEQGLDIVCIDSR

The following DNA sequence Seq-2366 <SEQ ID NO. 11> was identified in *H. sapiens*:

ATGGGCACCGCTCTCTTTAAAGTACACTTTCCTGACTCAGCTGTCCTCTTTTCCTCCTCC
ATTCCCACCAATTCTGGGCTACAGGCTTTTCCTCTACTCTCCCACAGCATCCTCCCTGAG
CCCTCAATCAAAGCACCTACAATACTGCCCTCATAGGGAGGTGCTATCTTTCTGTCTTTC
CCTGAGCGCTGGGACCCATTGCATTTCACCCATTTATCCCCAAGGCCTAGCACATGTCTA
GCACAACACAGCAATTAAATAAACCCTGTGGAATAAATTAATTGTGGAATAGCCTGGTTT
CCATGGATGGTTATACAGGTTGTGCACTGCACAACCATGTGCAACATTCCTGGAAAAAGA
CAGAAATTTATTGATTGGTTGGGGGTTTTGAATAGCCAAGGAAAACTATTTGACCATTGC
ATGCCCTCTACCTGGGAAAATCACATACCCTAACAACTTCTTAGGCCTTACTGCATGGTC
ACATGGGGTAACATTCATACAGTTTCTCCAGCTCTCTAGTCTGCCCACAAAGGTGATATT
GTTCAAAGGGGCAATCTTTCCTTGCCTTCCACCAGTCTATTCTTAACTTGACCCAAGTAA
TCTCTTTCACTGCTTACCAAAGATATTTCAGCTTCAGCTATCCTGTTTGCAGAATGGTGA
CGTATTCC

The following amino acid sequence <SEQ ID NO. 145> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 11:

MGTALFKVHFPDSAVLFSSSIPTNSGLQAFPLLSHSILPEPSIKAPTILPSGGAIFLSFPERWDPLHFTHL
SPRPSTCLAQHSNINPVEINCGIAWFPWMVIQVVHCTTMCNIPGKRQKFIDWLGVLNSQGKLFDHCMPSTW
ENHIPQLLRPYCMVTWGNIHTVSPALSAHKGDIVQRGNLSLPSTSLFLTPKSLSLLTKDISASAILFAEWR
I

The following DNA sequence Seq-2367 SEQ ID NO. 12> was identified in *H. sapiens*:

TCAATAGCAATAAAGCACACCAAGCACACAGATCTCGACTTTTGAATGCCACTTCTCCAT
CTTAAAAGACAAAAACAGGACATCTTAGACAAATGGCCAACTCCAGGGTGGTTGGGGCAA
GGAAAGAAGACGTGCTTGTGCACATCTTGGTACATCAGGTTTAGGAAGCTGTCACTGGTC
AAATCTGGGACAACTTGAACATCAAAATAAATAATCATTGTAATGGATTATAACTCATCG
ATGTAAGTCTCTAAGTACACACTTATATCAATACATATGTACATATACACATACATACAT
CTTTACATACTACTGAATGGCAACTAATAATGGCATTTGGCAAACTGTTATGCTAACAAT
TAACTCAGGCAAGAAACATCAATGGAGGCTAAAACTGGTAGATAAAATTGGGATGAGTAG
ATTTTACACAGTCTCCAAGTGACTTTCCACAAAATACCCATTATTACAAAGGAAAAGATA
GATAGGTTTGCAGCAGAAAAAAAAATGTCAGACATCATCTTAACTAGGGGATCAGTGTTA
ACTTCTCCAGCATGAGACAAGTAGACAAACAACTGCCATCAGAGAGGATGAAGTAAGACA
CAGCATCACTTCTGTGAAATTCTGG

The following amino acid sequence <SEQ ID NO. 146> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 12:

RISQKCCVLLHPLWQLFVYLSHAGEVNTDPLVKMMSDIFFSAANLSIFSFVIMGILWKVTWRLCKIYSSQF
YLPVLASIDVSCLSLLAQFAKCHYLPFSSMRCMYVYMYICIDISVYLETYIDELSITMIIYFDVQVVPDLT
SDSFLNLMYQDVHKHVFFPCPNHPGVGHLSKMSCFCLLRWRSGIQKSRSVCLVCFIAI

The following DNA sequence Seq-2368 <SEQ ID NO. 13> was identified in *H. sapiens*:

TCCGATGATGTTAACACCATATTATTTTTAAAGAACATGAAGATTACATAAGAGTAGGCA
TTTGCCTATTTGTATTTTTAAGAGTCTGCTCAGCTCTTAACAAGGAAGGGCCTATGCAAA
ATGAGAAATAAAGTGAAAAACGATTTGCTTGTCAGTCTGAAATAACTTAGGTGTCAAAAA

CAAGTAACTTTCACCCTCCTTCAACCTGTCCTCTTGCCATTTAGCAATCTAAAATAATTA
TCCAATGTATGGTTGCACTCCAAAAATCATGTTAAACTTGAGATATTCTGAATTTTGTGT
ACAATTTTTGGTAGAGGGTAAGAGATAGAGAAAAATCTTACATTGTGTTCAGTGAATTCC
CAGACCTCGGGGGTAAAATAAGTGCAGGAAGAATCTCATCAGGATATCTCGGGCAATTTT
TCATTAGTACGCATGACAAGCTGTTTCACCACAGGCTATTGTTTTTATGGAAAGTTCAAA
TATAGCAGGATGGGATGTATGGTGTGATATTAACACATATGAACACAATTATTACCTATT
TTAGGTATATACGACCTTTGTCACCTAGAAACATTGATACTCTTCATTATGATGTACTTT
TATAGAATAAGATAAA

The following amino acid sequence <SEQ ID NO. 147> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 13:

YLILKYIIMKSINVSRQRSYIPKIGNNCVHMCYHTIHPILLYLNFPKQPVVKQLVMRTNEKLPEISDSSCT
YFTPEVWEFTEHNVRFFSISYPLPKIVHKIQNISSLTFLECNHTLDNYFRLLNGKRTGRRVKVTCFHLSYF
RLTSKSFFTLFLILHRPFLVKSADSKYKANAYSYVIFMFFKNNMVLTSS

The following DNA sequence Seq-2369 <SEQ ID NO. 14> was identified in *H. sapiens*:

GGCCTCTCTGAAGGGGAAGCAAGCTTGCATCTAGACTTCTTTCTAAAGATAACCTAGACA
ATAATGAATACAGCTGCCACCAGCCTCCTATGCACTAGAGGCATTATTCTAGGAGTTTCC
GTGTATTAAGCTTATCCTGAAATTAGTTCCTTCTTATGACTGAGAGGAGAAGTATTACAT
ATTGATTTCATTGTTAGAAATGGGAAAATTTTTAACAAGTGTATTTAGAGGGCAACCACA
TTTTCTGCTCTGCAACCTGCTTCTCCCCCTTCACGTCAGGACATCTAGATGAACCCACTC
TTCGGAAAGGCTGCAGAGAAACATGTCCTACAGACCTACTATCATCTGGTTAACAACTCC
CAGTGGACGGACCAAAATTCCAGACGCTTCCCACTTTCTCTCCACTGCACGGATGCTGCC
ACACATGCTCATATACCTCTGAACCTTCCAGTGACTACGGCACAGCGACAGCTGAGTTCC
TGGGCGCAGAACCACTGGGGCACGTTTTGGCAGCTATGAGCAAATCACTGTGCACAAAGG
CAATCCCAGTTTACACTTCCACAGAGAGGAACTGAATACACTGCCCACCCTCACCTGAC

The following amino acid sequence <SEQ ID NO. 148> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 14:

GLSEGEASLHLDFFLKITTIMNTAATSLLCTRGIILGVSVYAYPEISSFLLRGEVLHIDFIVRNGKIFNKC
IRATTFSALQPASPPSRQDIMNPLFGKAAEKHVLQTYYHLVNNSQWTDQNSRRFPLSLHCTDAATHAHIPL
NLPVTTAQRQLSSWAQNHWGTFWQLANHCAQRQSQFTLPQRGTEYTAHPHL

The following DNA sequence Seq-2370 <SEQ ID NO. 15> was identified in *H. sapiens*:

AATACTAGATTCCTTCAGGGACTTTTTAGAACAAGGACAAGAATAATCCTTTCTCGACAA
AGTAAGGAGTGATCTATCTCAAGGCAGAAGCATATTCTCCTACACCAGGAGGAATTTCCA
TTAACATAAGCAATGCCCCAAGGATGCTTGTTATCATTTTTATTCAATGTTGTTTTCTGT
GTTCTGGCCAATATTATGACTTGAGATACAAGTGAGAAAGATGACTAAAGGAATTCATGA
GACAAGATGATCACTATTCAGGAGATGGTATGATTGTCTATCTAGAAAAAAAGAAATGAC
TCCATCGTAATTCTGGGAATTTACTAACAGTGGCTGGGTCCTGGACAAACATTTAAAAAA
TCAATCGTTTCCTTGTGTGGCAGCAATAACCATTTAGAAAATGGAGTAAATGCGGAGTTA
AGGGGCTGTGAATATATAACAGCAAGAACTCCTGATCTGCCGTCCCGACAAGTCGCCTCC
GGAGTGGACACCGGCCAGGGAAGGCAGGTCTCTGGAGGGAAGGTAGAGAGAAGATACGGA
GGATCTGCCCCTTCCCCAGGAAGCTCCCCGAGAAAGGGCCACAACTGTTTACTCCAGCAG
GCTCTGGGGGGATTCAG

The following amino acid sequence <SEQ ID NO. 149> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 15:

ILDSFRDFLEQGQESFLDKVRSDLSQGRSIFSYTRRNFHHKQCPKDACYHFYSMLFSVFWPILLEIQVRKM
TKGIHETRSLFRRWYDCLSRKKEMTPSFWEFTNSGWVLDKHLKNQSFPCVAAITIKMEMRSGAVNIQQELL
ICRPDKSPPEWTPAREGRSLEGRREDTEDLPLPQEAPRERATTVYSSRLWGDS

The following DNA sequence Seq-2371 <SEQ ID NO. 16> was identified in *H. sapiens*:

GAAAACCTTTGACTACTTTCTCTGTCTCACGGTCATGATTCCCCACATCTTATTCTAATA
TCTTTTCACCATGCTCTTAACAGCCATCATGACAACATAATACTTTTAAAGGATTGGGCT
TAATTGGACACTTTGGAATGAGTGTCCCCTCCTACTCCTCCTCTAGTTGTGTTCAAAAGT
CAGTTAGAGGTGTGGAAATGAAGTGATTGTGAAAAACTCTTTCGAGAAGTTCTGCCATGA
AAGGAAGTAGAGAAATGGGGCAGTAGCCAAGGGAGAAAAAGAGCTTGATGAGTTGCATTT
GCCTATTTAATAGAAGAGAGAGCAGAGTATGTTTGAATACCATTGAGAATGTTTCAATAA
AAAGAAAAAATGGAGGGGATGGGATCTAGAGGACAAATGACAGTGCTAGCCTTTGAAAGGG
GTTTGAATTCTTCAGCCATTGTAATAGGAGGGGAAGCAGAGCATGGATATGGAATCAGGG
ATAAATACCTATTAGAGGGCTGCTGTGAAGATTTCAGC

The following amino acid sequence <SEQ ID NO. 150> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 16:

LKSSQQPSNRYLSLIPYPCSASPPITMAEEFKPLSKASTVICPLDPIPSIFLFIETFSMVFKHTLLSLLLN
RQMQLIKLFFSLGYCPISLLPFMAELLERVFHNHFISTPLTDFTQLEEEEGTLIPKCPIKPNPLKVLCCHD
GCEHGEKILEDVGNHDRETEKVVKGF

The following DNA sequence Seq-2372 <SEQ ID NO. 17> was identified in *H. sapiens*:

ACAGGGCATCCTCGCCTTCCACCCACTTTAAAACAGCCTGCAAGGCAGTGTGTGACCTAT
GGCTTTAACTCTGATGAGGAGGATTCCTCATGGCATGGGTTGCTGAGAACCCTGAATCAC
AAGGTATAAAGCAGGGACCGAAGGACTGTGCCCACTGCAGCAACCCCCCGCTGGGTTTAA
TGCTCTCCTGTTGCCACCCTGAAATTTTTAAAGACTTTTTACGGGGTCTTGCTCTGTCAT
CTAGGCTGGAGTGCAGTGACATGATGTCTTATACCTCATCTGGCTGAGACTCACTAGAGA
AGGTCACTAGTTAGAACTAGAGAGGGGGCTGGGCACAGTGGCTCATGCCAGCACTTTGGG
AGGCTGAGGCAGGAG

The following amino acid sequence <SEQ ID NO. 151> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 17:

TGHPRLPPTLKQPARQCVTYGFNSDEEDSSWHGLLRTLNHKVSRDRRTVPTAATPRWVCSPVATLKFLKTF
YGVLLCHLGWSAVTCLIPHLAETHRRSLVRTREGAGHSGSCQHFGRLRQE

The following DNA sequence Seq-2373 <SEQ ID NO. 18> was identified in *H. sapiens*:

CTTGTAGCAATATAAAGCCTTAAATTTTTTTTCTGTAGGAAAATATCACACAGATGGCTA
ATTATATGCCATATAAAGCCATTAAGGAAGAAAGGATGGCAAATGCTCCTTTTAGTGAGA
CTTCTTTGTTATGAGATCTGGGTATAAAAATGTGCAGGTGTGTAAACAGAGGAAGGAGAA
TTCTGATTAAGTCCCTCAAGAATTGAAGAAAATGGGGTGAGAGACAGAGAACAACTGTGA
GCTAGGAAAGCTCAAGGAGTAAACCTAACAAGAAAGTTTAAGCAATGGCTACTTTTATAC
AGTTTATTTTAGTAAGTGCAAATACTTAAAATGAAGTTATTTATAAAGTTTATTTGAGTT
GTTTTCTGATAATTAAATAGCATGAGAAATGGGAGGAATTTGAGATATTGCAGTTAGAAA
GGGAGCAGTGCACCAAACTTATTCTTAACTTAAAAGTTCATACTCTTACCTAAGGTAAGT
CCTAATGTGACACCAACTTAAAGCTGAATTAGACAGGAATATTGCAATGAATAAGCAATG
ACTATTCACAATCTACTCAGCATAAAACAGGTTCATTAAGAAAGGTTCTGCAATAACACT
CTATGTAAGAGTTTATGGAACAATTAATAGAATAAAATTGATGTACATTTTATGTACTAC
TGCATTTTACATATTCTAAGGCACGAG

The following amino acid sequence <SEQ ID NO. 152> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 18:

LVAISLKFFCRKISHRWLIICHIKPLRKKGWQMLLLVRLLCYEIWVKCAGVTEEGEFLSPSRIEENGVRDR
EQLARKAQGVNLTRKFKQWLLLYSLFVQILKMKLFIKFIVVFLNSMRNGRNLRYCSKGSSAPNLFLTKFIL
LPKVSPNVTPTSIRQEYCNEAMTIHNLLSIKQVHERFCNNTLCKSLWNNNKIDVHFMYYCILHILRHE

The following DNA sequence Seq-2374 <SEQ ID NO. 19> was identified in *H. sapiens*:

CCCTTGAGCACACACAGGGCGATACTTGCCACAGGTGGGGACTGAAGGCTTCTTTCTTGG
CTTATAGTTTGGAAGCAATGGGAGTTGGGAGCTCCAAATCATTCATGGGACAAATATCCT
GTCTTATATTGCTTAAAAAAAAATCCTATCTAATTTTTAAGACAGGGTGTTTTGCTCTTA
AAGCACTTTGCATTTAATTGTGTTAATTACAGAAATTTTCAATGCTCTCTGAAGAGGTAA
TTGATATTAACCATGGTAATTCTAATAGCTAACACATATTGGGCATACGGTTTTTCACAT
GTCTAAACAGTCCATGTTTCCTTAAAAATGCAGATTGCAGGGCCCCACACTGGCTGGGGA
ATTCGCACTTCCAGTAAACACTTCAGATGATTTTCATGATCTTTCAAGTTCGGGGAAAAT
GGAGCTCGTTTTCCACTAGATTAAAGCAGTATTCCACTGTATGCGTTCTCAGGCCCTAAA
AGAATCAACACTCCTCAATAAGTAAACATTCACTTAAACATATCCAGGTGGATCCAATGA
TCTACC

The following amino acid sequence <SEQ ID NO. 153> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 19:

VDHWIHLDMFKMFTYGVLILLGPENAYSGILLSSGKRAPFSPNLKDHENHLKCLLEVRIPQPVWGPAICIF
KETWTVTCEKPYAQYVLAIRITMVNINYLFREHKFLLTQLNAKCFKSKTPCLKNIGFFFKQYKTGYLSHEF
GAPNSHCFQTISQERSLQSPPVASIALCVLK

The following DNA sequence Seq-2375 <SEQ ID NO. 20> was identified in *H. sapiens*:

CTGCTCTATATAAAGATATAGTCCATGTATATGGCTGAGTCTTTTATAGTCCAAAATGTA
TTTTTCTGTGTACTATGGTTTATTAACTTGACTTATTTTTCTTCTTTCAGATTTAAAAAA
TGTTAACTAATTAAAGTAACTTCCCAAGTACCTACCAATGACATTAATCTTCCTCTTTTT
GTCGTTTGTTCTTTTTACCCCCAAATCCTATTAATACAGCAACTTTTTAATATGATTGTC
TACTTTTCAGAGTACTTCTTAACAACATAGCAAATGCCAAAATGTTAATGGAAGTATTAA
TGAAAACATGCAAAAAATATTTCTTTATGATTCTGATAATTATTGAAATTGCCTTAGATT
AAACATGAATAAATTTAATTATTATATATGTATTCAAATAGTTGGATATATAGTCCTGAG
AAAGAATCCTTCACTACATATGTTATAAAAATGGGAATGAACACATTACCTAAGAAGTCT
GCACTAGAAATAATAAGATACCTTTTCATTCTTGACATCTTTCTTCTTTTTGAACCAAGT
ATCTGTA

The following amino acid sequence <SEQ ID NO. 154> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 20:

QILGSKRRKMSRMKRYLIISSADFLGNVFIPIFITYVVKDSFSGLYIQLFEYIYNNIYSCLIGNFNNYQNH
KEIFFACFHYFHHFGICYVVKKYSEKTIILKSCCINRIWGKEQTTKRGRLMSLVGTWEVTLISHFLNLKEE
KVKLINHSTQKNTFWTIKDSAIYMDYIFIS

The following DNA sequence Seq-2376 <SEQ ID NO. 21> was identified in *H. sapiens*:

TATCATGCTGCCGCTTCCAATGGGCATCTGTTCCACCATGTTGTGGGCATTCATTGGAGC
TTTGTTGCTTCTCACTGTTAAACCCTCCTGTATAATTCTGGGGTCCCAGCAGAAAACAGT
ATGTTACCCTAAAATAGGGCAATTGAAGGATCTTTCAAGAAGGGACAAGTTGTAAAGGTG

GGCAGCACAAAGGGAAACCAACAAAAAATGAAGACCTGGTGGGACAGGGACAGAGTGACT
GGATGCTGGAGAGACCCAAAGCTGCAAAGGAAAGGAGCAAGGGGAACAATACCCCACCCT
CTCCCCTCCCACCTCCCACCTCCCACCTCCATTCTTCTCCAGTGGTGCCGCCCATTGGGC
AAACCCAGCCAGAAGCCAGGAAGCATGAGAGTTCAGCTGATGCAGCCCATACAGATCAGA
CTCCTGGACTTCAGAGTGGGGGAGGGTGAGAGGGATGAAGTCTGGAGGCACCAATTGGGA
AGGCCATCCAGAATGCTCCTATTCTGTTTGGGAGCTGGGGATGGGAATGTCCCTTCCTGA
GGGGTATTTATGGAATAAATCAAATCAAATCACAGAAATCAAATCACAGAAATCAAAGCT
GGAGATTCTCTCTCCCTCTACTTGCTGGCAGCCAGGATGTGGGCTCATGACCTAAACTCA
GTCATTCAGAAATTCCCCCGGGGAATGCAGTCTTACAGGAGTAGCTCAAGGCCAGGCAGT
GGCTCACACCT

The following amino acid sequence <SEQ ID NO. 155> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 21:

RCEPLPGLELLLDCIPRGNFMTEFRSAHILAASKRERESPALISVIFLFDLIYSINTPQEGTFPSPAPKQN
RSILDGLPNWCLQTSSLSPSPTLKSRSLICMGCISTLMLPGFWLGLPNGRHHWRRMEVGGGRWEGRGWGIV
PLAPFLCSFGSLQHPVTLSLSHQVFIFCWFPFVLPTFTTCPFLKDPSIALFGNILFSAGTPELYRRVQEAT
KLQMPTTWWNRCPLEAAA

The following DNA sequence Seq-2377 SEQ ID NO. 22> was identified in *H. sapiens*:

CCCATCTGTCTGAATGCCTCCTGTAGTGGGGGACTCACTCCCTAATGAATCAATCCCTCT
TGTCTTTGGAAAGGTCTTCCAACTGAACTGGACTCCAACATCCAGTGAAGCTCCTCCACT
CATCCTTTTAGCTGGACCCTCTGGGGACCAAGACAGCAGACCAGCTGCCTCTTCTACAGG
GCAGCCCTCCAAATGGCTGGGGCCACTGTCTTCTCTGCACTAGAAGACCTTTCTATGGTA
GTATCCTTCCACATAAGCTATGACTTCTATTCCCAGGAAAGCCTGATTTGTCTCCTCTAA
ATGCACTTCCACTTATCTGTGACCCTCTTACAATGAAATCAGAGAGAGATAACCCTGATC
TTCTAACTCAGAGCAAGCAAGCTCCCAGGTCTTCAGAGGCCCTGCAGGGCACACAGATGA
CAGCGGATGACCAGAGGGCACATGCCTTGTCTAAAGGGGATG

The following amino acid sequence <SEQ ID NO. 156> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 22:

PICLNASCSGGLTPINPSCLWKGLPTELDSNIQSSSTHPFSWTLWGPRQQTSCLFYRAALQMAGATVFSAL
EDLSMVVSFHISYDFYSQESLICLLMHFHLSVTLLQNQREITLIFLRASKLPGLQRPCRAHRQRMTRGHMP
CMHFHLSVTLLQANLKGM

The following DNA sequence Seq-2378 <SEQ ID NO. 23> was identified in *H. sapiens:*

TTTCACCACTATGTAGCCTAAAGTTATTCCGTCATCCATGACTATCCTGTCTAAAGAGTC
TGAAGATCTTTATTTGGTAGCTATGGCTTCAGCTAGTTCATTTGCTAAGTTACCTAGAGT
GGTTGACAGATTTCTAATTATACGTTCATGAGAGGTTACTCCCCACTATTGCAAGAGACT
TCTGCCAAACATAGGCCAAAATTCATCTCCTTGGTTTGCAGGTACAGTTTGTCTAATCCT
GGAAAATAATTTCAATGAACTACTTCAGCGTTCAGAAACATTGGAGTTATAAATAGAAAG
AGGAAGAGCCACATAACCTAATAGACAATTACCTCTCATATGCCAGTGGTCAACACATTC
ATAAGCCCATGTGTGCTTGATCCAGGGACCACACAGGGTCCCTGATGGATTCTGAAATTT
AAGGCTTTGGATTACTGGTAACAGAGACATGTTAAAGTACATGTCTTCAGTCTTGAGTAG
AGTGTAATCAGTCTGATTTCTTTTTTTTTTTAATGAGACAAACATCAGGTAAAGACCTTG
ACAAGAAGGAAGAGAAATCCCGAGATTCTATAATCATAATAATCGAATTGTAATTGCTAG
TTTAAGTAGTCCTTCAAAAATACATCTCATTCCTGACAGGATAAAACAAGTTTTATAAAA
TATATTATATTCTGGGTTCACTAGGGGAACAC

The following amino acid sequence <SEQ ID NO. 157> is the predicted amino acid sequence derived from

the DNA sequence of SEQ ID NO. 23:

VPLVNPEYNIFYKTCFILSGMRCIFEGLLKLAITIRLLLNLGISLPSCQGLYLMFVSLKKKRNQTDYTLLK
TEDMYFNMSLLPVIQSLKFQNPSGTLCGPWIKHTWAYECVDHWHMRGNCLLGYVALPLSIYNSNVSERSSS
LKLFSRIRQTVPANQGDEFWPMFGRSLLQWGVTSHERIIRNLSTTLGNLANELAEAIATKRSSDSLDRIVM
DDGITLGYIVVK

The following DNA sequence Seq-2379 <SEQ ID NO. 24> was identified in *H. sapiens*:

CCTTCCTCATCTTTGCTGCTCTCTGCTGACAATTTAAAAACCCGACATGTGTTAACTCTC
TCCTTGTCTTCCAACCCACCCACTTATCACCTCAGTGCCATGCTCCCAGGTGGCAAGCAG
AGAGGACTGTGGTTTGATGAGTTCATTCATGCCGTGGCTTTAATTACTGATAAGAGCTTG
ATTATACACATTCTCAAAGGCATTGGAAAGTTAAAAGAAAGTCCTTTTAGGTAGCAGTCC
ATGACAAATGCAGTTCATGAAATCTGTGTCCTTTTCATTCCCTTCTGAGTAATTCCTCTC
TGTCTCTATCAAAGCCTTGGATACTCCATGGTTTACTAGGCAGAAACTTATCCATCCAAC
ACAGCCACATGGATACAGCTTTGTGCTTTTAGACAATAACCACTTGAGAAAACCTGACCT
TTTCCCCCACTCTTCATTCAGCTTCTGTCCTGCTGAAAACAAGAGGACATCCTGCCACAT
TGTCATCTGCTCTGCCTTACTCTTGAGAAGTCTAGTTGGGAAAACAGGCCCTATAAAGAG
AGACACTGCAATGCCATGGGGTGAGGACAATAAAAGTGATGGCAGCAGAGCACTGGAGAG
CAGAGGTGGGGTCACCAACTGCCCAAATGGCACTGTCCCCTCAGAACTCTTGCATTTGCT
TTTAACGCA

The following amino acid sequence <SEQ ID NO. 158> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 24:

LPHLCCSLLTIKPDMCLSPCLPTHPLITSVPCSQVASREDCGLMSSFMPWLLLIRALYTFSKALESKKVLL
GSSPQMQFMKSVSFSFPSEFLSVSIKALDTPWFTRQKLIHPTQPHGYSFVLLDNNHLRKPDLFPHSSFSFC
PAENKRTSCHIVICSALLLRSLVGKTGPIKRDTAMPWGEDNKSDGSRALESRGGVTNCPNGTVPSELLHLL
LT

The following DNA sequence Seq-2380 <SEQ ID NO. 25> was identified in *H. sapiens*:

AATTTATGACATTATGACAGTTTGTCATTAAAGATAACATTCCAAAGAGAAATGGGCATG
GGCATATATTTACCACTCCCAAGGAAATAGCTAATAAAGTAATAGAGTACAGATTAAAAT
AATAAAATCCAAATTTAATCCATCACATTGACAATGATTAAAATTAAATTTAAAGCAGTG
TTGGGAAGAATACAGTGAGCTGGTGTCCATACACACTGTGATGAGAGTGTAGAAATCTTA
CAGTCTTACCAGAAAGCAAATGTATCAAACACTTTCAAAATGTTCATACTTCCTAACCTA
GAAATTCCACTTTTAAGAATTTCTCCTAAGAATATATCTTTGTTTAAAAATATTTACATA
CAAAGATGTTGATTTTAGTATTATTTTGAAAGCAAAATAACCCACAGAATCTCAAGTATA
TGATCCAAACAATGGAATATCTTATAGCCATTAATTTTAGAGATGAATATTTAATAATTT
AGGAAAATACCTATGATACTTTAAATTTTAAAAAGTTACATAGCAGAAGAGGCCATATTT
CAATTTTTGCCTTGGAAAAATATGGTATCACTACAGAAATGTTGTAGTGTTATCGCTGAC
AACACTAGTTATCTAGGATAAAGGATATTCTCATTTTCATTTCACCTTTAGTA

The following amino acid sequence <SEQ ID NO. 159> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 25:

LKVKKEYPFILDNCCQRHYNISVVIPYFSKAKIEIWPLLLCNFLKFKVSVFSIIKYSSLKLMAIRYSIVWI
IYLRFCGLFCFQNNTKINIFVCKYFTKIYSEKFLKVEFLGEVTFKCLIHLLSGKTVRFLHSHHSVYGHQLT
VFFPTLLIFSLSMWIKFGFYYFNLYSITLLAISLGVVNICPCPFLFGMLSLMTNCHNVIN

The following DNA sequence Seq-2381 <SEQ ID NO. 26> was identified in *H. sapiens*:

CCAATATTTGATCTTTTCTATCTTTAAAAATGGCAGTTTCATGTGTCTTGATCTAAAATC
TTAAAATCAATCTTTCAATTGGATAAGAGGCAGGGAAATTAGCTTGGAAGGTAAATCTAT
TATCCAGAGGCAAAATTTCATGGGCTTTGATAAAGGTGGATATTTTTCGATAAGGAGGAA
AGAGTAAATTTTACTAACATACTTTGGCTTTTGTTCAGTTTTCTTAACCTCTATTTTCGC
TTTATTATTTATTTTTTTGTTTTACTCTTGGGAAAGCAAATTATTTGTTTTCTCACATCT
TTTGGGGTCCAATTTTGATGATTCTGATCTTTTTTAGTTGCTTGACCTGTAGACCCTCTA
CAGAACATTGCAGGGCCTCTTCTCAGAGGAGCAGCGGTGATGAGCTTAGTTTCCTAGGCT
GGGACTGTTGCGCTGGACTTGACAGGTGAACTGAAAATTGCAGGGATAAGTACACCTATT
GAGAACAAACATCCCATCTCTTTATCAAAGCTCTTCATTGGCTTTGGAAAACTGCTGTAG
GCCTAAGGAAACTAAACTTTCTAGGGATATTCTAGGTTTTAAACATATGAGAAAGAGAAA
GACGTCGGTTCTTATTTAAGAGAGTTTATGAGACCTTATCCTTGAAATAGTCAAATTTAT
AAATGACATAAGGCTGTATGTGTAGTT

The following amino acid sequence <SEQ ID NO. 160> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 26:

NISFLSLKMAVSCVLINLKINLSIGEAGKLAWKVNLLSRGKISWALIKVDIFRGGKSKFYHTLAFVQFSPL
FSLYYLFFCFTLGKANYLFSHIFWGPILMILIFFSCLTCRPSTEHCRASSQRSSGDELSFLGWDCCAGLDR
TENCRDKYTYEQTSHLFIKALHWLWKTAVGLRKLNFLGIFVLNIERERRRFLFKRVYETLSLKSNLMTGCM
CS

The following DNA sequence Seq-2382 <SEQ ID NO. 27> was identified in *H. sapiens*:

ATAAAATACAGATCTGATTGTGTCACTCTCCTGCTTAATATTTGTAGTTGACCCTCCCAC
TGCTCTCATGAAAGTTCATAATCCTTACTGTGGTTGTAAATGCCCTTTTATGATCTGTCC
CTTGCCCATTTGTGTACACTCATCTTGTGCTACTCTCTTTCTTCATCAATATGCTCCACC
ATACTGTCATCTTTCTGCTTATTTTTTTTAAAAAAGTATGGAACATCTCTTTCCCCTTAT
GTGTCTTATGCAACCTGTCAGACAAAACCACATGTTATATTTTCTCAACACACAATTTTA
TTTCAGGTCTCTGTGCCCTTTACAAATCTACTAATCTTTCTGTCTGGAGTGTTCTTTCTT
CTCCTGGCCAAATTCTAATCATTTGTCAAGAGTGCAACAGCATCATTTCTTCTGTGACTC
AATTCTCCAAGCATCGTATCCTCTGTGTTCCTATAGCACTACATTGGATCGGTCCATAAC
AATTCTGTCAGTGTATTATAAGAACTTATTTACAGGTTTTGTCTCTTCTACTATGGCGTG
AGCCTTTTAGTCATATGAATTGTGATTTTGTATATTTAGCGCCTACCATGGTGCTTAATT
CGTGGTAGGTGCTCGGTAAATG

The following amino acid sequence <SEQ ID NO. 161> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 27:

KIQILCHSPAYLLTLPLLSKFIILTVVVNALLSVPCPFVYTHLVLLSFFINMLHHTVIFLLIFFKKVWNIS
FPLCVLCNLSDKTTCYIFSTHNFISGLCALYKSTNLSVWSVLSSPGQILIICQECNSIISSVTQFSKHRIL
CVPIALHWIGPQFCQCIIRTYLQVLSLLLWREPFSHMNCDFVYLAPTMVLNSWVLGK

The following DNA sequence Seq-2383 <SEQ ID NO. 28> was identified in *H. sapiens*:

CTATTGGTTTAATAAATTATGGTATAATCAAATAATGAAACTCTATGCATTTGTTAAAGT
AACTTTTCAAAAGAATATCTTGTAACATAGAATAACAGATCCTAGTGCATTACCCACTCT
TTGGGCTTTATCGCTTTTCCACCATCATTATCTGCATCACTGCCTGCAGGTTTTCTACAC
GGCCAGGGTTGGTCTCTGCCTGCTCAATAGTCAAGTCAAAAGAGGCAGGAAATTAACACC
CTCTGGAGGCAGCCTTTGAGGAATGATCCATGGGAGGTGGAGTATAAATACCTCAGCTCT
GTTTCCTCTAGAGATATAACTAAGGAATGGGTTTTACATTGTTTCTCAGAGTTTCCTCAA
GGTTTTAAACTTCAATCACCCACAGGGGTAGTGGGCTTTATCATAGTATACATCCTTTGT
GGCTTCCCTTCCTTCTTGTCTCACTTCTCCATTCCAAACTAGGATTTATTTCTTTTCCCT
AAAACAAAACAAAATGTTTAACCTGAAACCCTTACAAAACACGTAAAATTTATATTTAAA

AAATCTAAATATTTGAGGAGAGAACGAAACCTAAGTATATGCCCAGGTATAACACGATTG
GTGGAGATAGCTTTAAAAAAGTTCCTGAAAAATTTAGTTTTTAAAAGGGTACCCTAGTAG
AAGGTGACTTAACTGCCTAATTTC

The following amino acid sequence <SEQ ID NO. 162> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 28:

YWFNKLWYNQIMKLYAFVKVTFQKNILHRITDPSALPTLWALSLFHHHYLHHCLQVFYTARVGLCLLNSQV
KRGRKLTPSGGSLGMIHGRWSINTSALFPLEILRNGFYIVSQSFLKVLNFNHPQGWALSYTSFVASLPSCL
TSPFQTRIYFFSLKQNKMFNLKPLQNTNLYLKNLNIGENETVYAQVHDWWRLKSSKIFLKGYPSRRLNCLI

The following DNA sequence Seq-2384 <SEQ ID NO. 29> was identified in *H. sapiens*:

CTGGCTTCTGAGAGCCTCCTGGTTAGGAAGGAAGTTGTTCTCTTTCCACTGCAAGCTTAG
AAAGCCTTCCAAGTTCTCTCCTTCTGCAGCATAAAGAGACAATAACTCAGAGGAAGGTAT
CCCCAGGAGTTTCCAGACAGCTGCACAGATTTAAGTGCAGAAATCTGAGCAGAGGTATAG
TCCTGGCATTTACATGAACACCTTTCAGTAGCAGGAAGAATAAATGGAAAGAGAGCTACA
GAAATACCAGGGGCGAAGTCTTCATCTGAAAGTCCAATCTTTGATCAAGAGCTGGTAGGA
AGTCTGAGAATTTGTATCAGCAGTGATTCTAGGCTGTCTGGTCTGAGTAATTGGGATCAG
AGCAACAGCTGATATCATGCTTACCTTGTGCCAGGCTCCCTTCTAAGGGCTTCCTGGACA
CCTGCTCGTGTCAGTCCTCACAGCAATCACATGAGGTATGTTCTGTTGTTGTCTCCTTGT
GCGGATGAAGACACTAGGCACAGAGAAAACTGGCCACAGGTGTACAGCTGGGGAGGCCAG
AGCCAGAATTCAGACCTGGGGTGTCTTGGCTGATGTGAGCTAGTGTGGGCCAGCATGGGA
CACAGAGGGAGGATTAGCTGGAGAAGCAGGACAGAGGGCAAGAGAGACGAGATCTCCGAC
AGTGCTGGGTCAGAGACACTTTCCTGAGCCATGATTAAACCTGATTATGGACATGTTTT
AGCCTGTCAGA

The following amino acid sequence <SEQ ID NO. 163> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 29:

LASESLLVRKEVVLFPLQAKAFQVLSFCSIKRQLRGRYPQEFPDSCTDLSAEIAEVSWHLHEHLSVAGRIN
GKRATEIPGAKSSSESPIFDQELVGSLRICISSDSRLSGLSNWDQSNSYHAYLVPGSLLRASWTPARVSPH
SNHMRYVLLLSPCADEDTRHRENWPQVYSWGGQSQNSDLGCLGCELVWASMGHRGRISWRSRTEGKRDEIS
DSAGSETLSAMIKPDYGTCFSLS

The following DNA sequence Seq-2385 <SEQ ID NO. 30> was identified in *H. sapiens*:

ACAGTGAGCAGAGATGGAGTCACACCTTTTCACAAAATTTAACAATCATCATCGATATGC
ACAGCCTTCATGTGTAGTGTATGCTCCCAGCTACAGCTGTAGTTACCCAATCTCAAAGCA
AGTAAACAGCAAGATTCCACACTAGCTCTTAACTGGCCAAGCTATATTTCTATAACTAGA
ATTGCTATTTGTGGATTTCCATAAGTTATAATAACACGATAAGACCACTTTATCCATGTA
TTCTAGTGACTTTTTCTTCCTATAGCAAAAAGAAAAATACATCTTTCACCATTTACAAGT
ACAAATTTCAAGGAGAAATTTTAAAAGGAGAGTAACAAACTGTCCTGAGTTGCAGCAAGA
CTCCTGAGAGTTCCATTTCCTGGGCCCTCTGCTGCCTGTTTTTGGCATTGAACCCAGGAA
TCTTTTCTAAAGCACACAGAAATCTTGCAAAAGAGGCCATTTCTAGTTAGGCTTTTGTCC
AACTGTCTAGTTAAATAAATTAAATTCTTAGATTACAAAATGTGCTTCAAAGGTTTAACA
AATTGAAATGTCCTTAAGTATTTCAAATAAATTAAGGAAGAATTCCCATTCCCATAGTCT
TCTACTTTCCTCTTCCACACCTATGATGAATGTCCTGAAAAG

The following amino acid sequence <SEQ ID NO. 164> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 30:

FQDIHHRCGRGKKTMGMGILPFINTGHFNLLNLSTFCNLRIFILDSWTKALEMASFARFLCALEKIPGFNA

KNRQQRAQEMELSGVLLQLRTVCYSPFKISPNLYLMVKDVFFFLLEEKVTRIHGSGLIVLLLMEIHKQFLK
YSLASELVWNLAVYLLDWVTTAVAGSIHYTRLCISMMIVKFCEKVLHLCSL

The following DNA sequence Seq-2386 <SEQ ID NO. 31> was identified in *H. sapiens*:

CCCTTTTTTCTGCTTTCAGTTTGATTTGATTACACCTTACAGGCTTGGTATGATAAGTTT
AAAACATATTGAAGGTTTATGTACTTATAAAAACCTCATCATTCCCTAAAGAAAAAAAAT
CTCAATTTGGTTTAGTGTCATTGTAGTCTTGCTTTCTACATCTTACTAATGTCTCATTTA
TTTATTCATTTTGCTCTGTCACATTTAGAATGATTTTGATGGGCAAAAATCATGGTAGTT
ACAAACAGCCCTTTAAAACTATTGTTATACTTTGTTCAGTGGATTCTGGTAGAGGCTTTA
AGGTAATTATTTCTTTAAAGCATTGTGTAAATATACCTCCTACTGTAGTGCCCTTGGGAA
CAGGCAAAATTCAGAACTGGCCTGCTAGCAGTCTTACCAGGGTTATAAAAGTAAGATTAT
TATATATAAAACAGCATTAACTCAATGCGTGGTGTGTTGCAGCTGGCAAACAACCTCGCT
CCCCAAGCTGCTAAATTCGTGGTCTTATGAATGTCTCCATTGCTGTGTTTGCTGTAACAA
GAAGTGGGAGGGTGTTCCCCAGTAGCCTTGACTGTTTACCAATGCACACTCC

The following amino acid sequence <SEQ ID NO. 165> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 31:

LFSAFSLILHLTGLVVNILKVYVLIKTSSFPKEKKSQFGLVSLSCFLHLTNVSFIYSFCSVTFRMILMGKN
HGSYKQPFKTIVILCSVDSGRGFKVIISLKHCVNIPPTVVPLGTGKIQNWPASSLTRVIKVRLLYIKQHLN
AWCVAAGKQPRSPSCIRGLMNVSIAVFAVTRSGRVFPSSLDCLPMHTGVCIGKQSRL

The following DNA sequence Seq-2387 SEQ ID NO. 32> was identified in *H. sapiens*:
TTATTTGGTGTTAATTTCATAGGCTCAAAGGTCTAAGGTGCCCCCCTGTTGCGGTTGCCT
GTGGTTCTCTTTGCTCCTGTCTGCCCTCTTGGGCCCAATACCTAGTATTGTGCTTAGGAT
TCACAAACGCAACAAATACTTACTGAGCACCTACTCTGTGCCAGGTGCTGTGCTATATGC
TGAGAAAACAATGTTAAACAAGATGGATAAGGTTTCTTCCTTATGGTGTCCATAGTCTA
GTGGCAAAGACAGGTAATAATGACTCAGTGTATTCTACTAAGGACAAGCATATCGTGCTA
AGAAAACCTGTGTGGGAATGGGTCAGGGAAGGTATCCTTGGAGTAGCCCCGTTTGAACTG
GGATCTGAAGACTGAGAGTTATCTAAGTGGGGAGAGCATTGCAGGCAGGGGGATCAGCAT
GTGCAAGGGTTCTCAGAAAGGAGGGAGAACAATGTGTAAGAAATATCACTGTAGTTGCAA
CCCAG

The following amino acid sequence <SEQ ID NO. 166> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 32:

IWCFHRLKGLRCPPVAVACGSLCSCLPSWAQYLVLCLGFTNATNTYAPTLCQVLCYMLRKQCTRWIRFSSL
WCPSSGKDRLSVFYGQAYRAKKTCVGMGQGRYPWSSPVTGIRLRVIVGRALQAGGSACARVLRKEGEQCVR
NITVVATQ

The following DNA sequence Seq-2388 <SEQ ID NO. 33> was identified in *H. sapiens*:

TCATTATTATAAGAATTATAAGAATTCTGAAATATTAGCCTTAAAATAACCAAGTTAATA
AAGCTTAAACTTTTTATGGAATTATCCATTTCTGTTTTGAAAAATACTGAACTCTTTTCA
AATACTATTGCTTGTTCACTTAACAATGATTACTTGAACATAGTTCAGCTAAAGCTTTTA
TGATATTCACTAATCTAGCATTTATTTTCGCATTGCTTTCCACCATCACTAAAGTAATTA
CTACATGTTCACCAACTAATTATTCTGATGGTGCATTAAGAATTGATCTTTACCTTAATA
TTTTATGGTATCAAGTGTTTTTGCATTCATCAAGAATATTCCATTTTGCTTATATTTTAA
TGATGAGCTCTAGAATATCATCACTAACATATCTAGCAAATTATAAATATGTCATTTTTT
AGGTAAAATATTTAAGAGTATGTAGTGCTATATATTTAGTTATTTTAAATCAAATACTTA
ATGTTTATACTTTTTAATTGATGTACAATTTTCAATTCTTTAGAATGCGCTTATGAAATA
ATTGCCCTTATTATAGTTTATAACAACTTTAATATATCTTCTGTATCTATAGCAGATGA

TTTATAAAAATGCTTTTCTTTATTAATAACTGTCTCTATCTCAAGTTCTTCATAGTGAGC
TATTTTTTCTTTTTGTATTCCTGTAGAGATACATA

The following amino acid sequence <SEQ ID NO. 167> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 33:

IIIRIIRILKYPNNQVNKATFYGIIHFCFEKYTLFKYYCLFTQLLEHSSAKAFMIFTNLAFIFALLSTITK
VITTCSPTNYSDGALRIDLYLNILWYQVFLHSSRIFHFAYILMMSSRISSLTYLANYKYVIFVKYLRVCSA
IYLVILNQILNVYTFLMYNFQFFRMRLNNCPYYSFITTLIYLLYLQMIYKNAFLYLSLSQVLHSELFFLFV
FLRYI

The following DNA sequence Seq-2389 <SEQ ID NO. 34> was identified in *H. sapiens*:

AGGCAGTAATTCCAGTAATGTGATGAAGTAGCAAGAGATAAGTAAGTCCAGGTCAGTGAA
GACTTCGTGGGGCTGACATATGAACTGAGGAAATGCCCACTTTTGGACTTTCAGTTAAGA
CAAAAATAAACTTACCTCTTTTTTTTTTCCCAGGTATCTGTTACTTTCCCTATTTTGCAA
TACTTAATGGATACATACAATCTGTCAACTCTTCTCTCTGGACCTGCGCATACACTGCTC
CATCTGCCTGAAACAATCTTTCCCTGGTCAACCGCCTACCCACTGCCACCTTGGAGAACA
GCTACTCATAGTCACCCTCAGATTATATCGTTTTCTCACCCATCTCATCCTCTTCCTTCC
CGTTTCACCACCTCCCTTCAACCTTGGTGGGCTTTGCCCATCTGTCTGCTTGACAGGACA
CCCCTATTGTTACCTTTGACTGGACTATTAGATGACATCTCAGTTACTTACCTTTTATGT
GCTAGAATTAATTTCCTAGCTGGAGTTGTCCCCATGACCTGAAGCTGAGTGCCTGCTCTA
CCATGCAAGAAGCTCTATTGCCGAGGCCTAGGCCTGTTTTGGGGGCTTCTCTAGCCAATG
TGCAATGTCCCATTCCTAGTTGCATTCTGAAATATAACATCTGAGTTCACAGTAT

The following amino acid sequence <SEQ ID NO. 168> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 34:

YCELRCYISECNEWDIAHWLEKPPKQAASAIELLAWSRHSASGHGDNSSEINSSTKVSNDVISSQRQGCPV
KQTDGQSPPRLKGGGETGRKRMRWVRKRYNLRVTMSSCSPRWQWVGGPGKDCFRQMEQCMRRSREKSQIVC
IHVLQNRESNRYLGKKKEVSLFLSLKVQKWAFPQFICQPHEVFTDLDLLISCYFITLLELLP

The following DNA sequence Seq-2390 <SEQ ID NO. 35> was identified in *H. sapiens*:

TTTCGAAAAAACGTATATGAAAGATTTAAAATATGAGTTATGATGTCTTTTTTTATCCCA
AATCTGCTTTAATTATCATCCTATGAGAACATTTTTGGACATGCATGAACATACAAGTGT
TCTATGTACCCTTCCACAGGAACTATTAGAGGTTAAGCATCATTCAGCCAAAAATGACTA
GACAAACTTCAATGAGAGGACTGATGTGAACATTTAAATATATATCAAGATAGATCTAAG
GTTAAAAATTATTGAGAATAAAATTGGAAGAACAATGTATCAACGTTATGCTATTCAAAA
CTAGAAATAATGCATGTAAACAATGGGAGAAGAAGGGAAAGTAAAAAAGACAATTGTAAA
AGCACGTTATTGGATAGCAAATGTATGGGAAGTAAAGTACACACATTAAACTTGGCAAAC
CAGCAGATAAGAAGTTACATAAGAATATAGATGGCTAATGACATTTATACGTATAAATAG
GCCTTAAAACAAATATTAAAACCTTT

The following amino acid sequence <SEQ ID NO. 169> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 35:

KVLIFVLRPIYTYKCHPSIFLCNFLSAGLPSLMCVLYFPYICYPITCFYNCLFYFPFFSHCLHALFLVLNS
ITLIHCSSNFILNNFPIYLDIYLNVHISPLIEVCLVIFGMMLNLFLWKGTNTCMFMHVQKCSHRMIIKADL
GKKTSLIFIFHIRFFE

The following DNA sequence Seq-2391 <SEQ ID NO. 36> was identified in *H. sapiens*:

GGCCGCCCAGGTCAGGGAACCGTGGTCTAAGTCCCAGCTTTATTCTTAGTTGGAGGAGTG

GCCTTAGGTATGTCACAGGGCCCCTTAGGCCTTTTGGTTGTCGTTTTCATAAAAGGCAGC
TTGTCTTGCTGCTGACAATCATCTTTGAGAGTGTTAGACTTAAATGAGATCCTGCAGTAG
TTTTCACCCTCCACAGGTAGCAAAATCTTTACTCTAAACAAATTGTACTTGATTCCTTGA
TGCTAAAACAAAAGAAAAACCTGGAATTTTATTACTACAAACATATTCTATAAGCCCTCA
TGTATATTTTTTACTTTTCTTGGAGCCCCTCAGTAAGAAAAACAAAACAGCTTTTAATAC
AATGTTTTCACAATGGCAAAGTTCAAACACAGACAAAGGTAGAGGCAATGGTATGATAAA
GCCCCAGGCATTCATCACCCAGATTCAATAATTACCAATTCATAATCAACCCAATTTCAG
CTCTCCACCTCACACCTCACTTTTTAAAAGACAGATCCTCCCTCATTAGATTAGTTCATT
CACAAATATTTTATATGATCTTGAAAATATAAGTGCTCCTTTAATCATTGTGATATCAAA
TTCAAAATTAACATTAATTCTCAAATAAATAGGGCTATTTTGATG

The following amino acid sequence <SEQ ID NO. 170> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 36:

HQNSPIYLRINVNFEFDITMIKGALIFSRSYKIFVNELIGRICLLKSEVGGELKLGLIGNYIWVMNAWGFI
IPLPLPLSVFELCHCENIVLKAVLFFLLRGSKKSKKYTGLIEYVCSNKIPGFSFVLASRNQVQFVSKDFAT
CGGKLLQDLIVHSQRLSAARQAAFYENDNQKAGALHTGHSSNESWDLDHGSLTWAA

The following DNA sequence Seq-2392 <SEQ ID NO. 37> was identified in *H. sapiens*:

TTTGAAAGTACATGTATAACTAATCTACATCTAGCATCAAATAACTACCACTTCTTCCTT
CCTGTTTATATCATTACTGCCTTTTATTTCATTTATCCACATGCTATAATCACTCAATAC
TTTGTTACTATTATTGTAAACAGTTATCTTTCAGATCAGTTAAGAAAAAATAAAACTTAAT
TTTACCTTAATATAGTACTTTTCTAATGCTCTTCCTTTTTTATGCAGTTCTTTTTGACAT
TTCTCATAGGGCAGGTCAGCTGGCAATGAATTATTCCAGTTTTGTTTGTCAGAAAATATC
CTTATTTCTTTGAATTTGAAGGATAATTTTGCTGAATGCAGAATAATAGTTTGGTAGCTT
TTTTGTTGCAACACTTCATGTATTCTCCTTTCTTTGTGTTTGCATGGTTTCTGAAGAGAA
AGATAATGTAATTCTTATCCTTTTTCCTCTATGGATAAGGTGTTGGCTTTTCCCCCTCTC
TAGCTTCTTTCAAGATTTTCTCTTCTCTTTGGTTTTTTGCAGTTTAAATATGATATGCCT
GGGTGGAGATTTGGATTTATTAT

The following amino acid sequence <SEQ ID NO. 171> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 37:

LKVHVLIYIHQITTTSSFLFISLLPFISFIHMLSLNTLLLLLTVIFQISEKNLILPYSTFLMLFLFYAVLF
DISHRAGQLAMNYSSFVCQKISLFLIRIILLNAEFGSFFVATLHVFSFLCVCMVSEEKDNVILILFPLWIR
CWLFPLSSFFQDFLFSLVFCSLNMICLGGDLDLL

The following DNA sequence Seq-2393 <SEQ ID NO. 38> was identified in *H. sapiens*:

ACTTCTAACTGCTGGCTTTAATTTAATTTAATTTAATTACAGCATTTTCCACACATGCCC
ACAGGCTCTTGGTAATAGTTGCATTTTTAATAAATCTAATATATAATAATGACTTTGTTT
TTAATTTTCCACTGAGAGTTGGATCCTGAGTTGAACACAGAGCTCCAGACAGGGGCGTCT
GGTTCACTCCATGTGATTGGATTTCAGGGAACCAAGGGGCTCCTAATTGGAAAATAGCTG
TGCTTTCACCCCCTATCCCCACACACCTGTGTTTAATGTCCTCAGCAAGCATCCCATAGG
ACATGAAATGACCGCTTGTTTCAGTCAAAATGATCAAACCAGTTGAGCAGGCATTCCTCA
GGCTGGACTGTGAAAGGAAAATGGAGGTAAGCGAGCAATGCCTGGCCAAGACCATTATAC
AAAGAGACTCTATGGACAGCACTCTGGTGGTGGCCTTTACGGAGTGACCCACTGCTCTCT
GCCTTTATCCACAAGTCACTGGGCCAACTTAGAACTGTAATCAAACATAGTTCAACCAAA
GGATGAATTTTATGACTACTGATTTCTCCTTTGCAAAGACCGTGGTTGATATTCATCGGT
AGGC

The following amino acid sequence <SEQ ID NO. 172> is the predicted amino acid sequence derived from

the DNA sequence of SEQ ID NO. 38:

AYRISTTVFAKEKSVVIKFILWLNYVLQFVGPVTCGRQRAVGHSVKATTRVLSIESLCIMVLARHCSLTSI
FLSQSSLRNACSTGLIILTETSGHFMSYGMLAEDIKHRCVGIGGESTAIFQLGAPWFPEIQSHGVNQTPLS
GALCSTQDPTLSGKLKTKSLLYIRFIKNATITKSLWACVENAVIKLNIKASSK

The following DNA sequence Seq-2394 <SEQ ID NO. 39> was identified in *H. sapiens*:

CTCGAGCAGTAACCTGTGCTTCTACAATTATGACACCCACTCCAGGGATAGTCACTGCCA
AAGGGTAGAACTGCTGGGGGCTCATTGCACTCACACAGACTAAGAGTGTAGCATCTCCCA
GTTATGCGGGCATCAGGGCAACATGGGGAGAACAGTGGCAGGCACATAAGGCCACCCCCA
GGTACAATGTCCAGTGCAGTTCACGGGTAGGTAAATCTACTCTGTGTCCCCACAGACCCA
TAGACTCCCAGGGGGCACAAAGTCAATCAGGGCCTGACCTTGGTAGTGACATGTGTTATG
TTTGCAAAGGCTGTGACAGGTACCCATCCCACAGTGGTGTTACCCCAATGTTGCTCTATG
CACTGTGGCACTTGGGCTGGGAGTACTACATGTTCCCCACTAGCCAGCCCCATCATAAAC
GCTATGGGCCAGCCAGGGGTTGGGCACACCATGTGTCTTGCAGCATCCTTTGTCCAAAGC
TGCCATGTTGCATTCCAGGCATCAGCCATGGGACCCCCAAGTCTCCAACCATGTCCAGTT
CTCTGCAGACACAAGATGTATGTGCCAAGGCAAGCCATCCGCAGCCCTGCTGGAAGGGCA
GTGCATATCCAATAGTTGGAAACATTGGTCACCTAGTGTAAGGTGTGGGCCCAGTCCACA
ATGCAATTGGAGTATGTTAACCTCTGG

The following amino acid sequence <SEQ ID NO. 173> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 39:

QRLTYSNCIVDWAHTLHVTNVSNYWICTALPAGLRMACLGTYILCLQRTGHGWRLGGPMADAWNATWQLWT
KDAARHMVCPTPGWPIAFMMGLASGEHVVLPAQVPQCIEQHWGNTTVGWVPVTAFANITHVTTKVRPLTLC
PLGVYGSVGTQSRFTYPTALDIVPGGGLMCLPLFSPCCPDARITGRCYTLSLCECNEPPAVLPFGSDYPWS
GCHNCRSTGYCS

The following DNA sequence Seq-2395 <SEQ ID NO. 40> was identified in *H. sapiens*:

AATTTTTTTTCACTACGGAAACTCGTTTGCTAATATAAATGCAGACTTTTTTTAAAAAAA
AGCTTTATTTGGAAACATGATGAAAAATGTGATGTATTAATACTTACTGATACTCCAAGA
AAAAAATAATAAAATATTTAGAAAGCTCCTCCCATCATTTCCTTTGGCTTTTTAACTCTA
CCAGATCTTTGAGAATGCATATTGTTGCTGGTTAACCAGATGAACCACCCTTTCCTTACT
AGTTCTGCAAGATTCAATATCATTCATAGTCTCCAGCACTCTAGAGTAATCATTACTAGC
TGTTAGGAAAATTATGGTATTTCCTAAAAACTTTCTTTGTGACAAGTGAATAAACCAAAA
GGATTAAAAAAAAAGATGTTCCAGTTTGGGAAAAATAATGCAATGAATACTGCATCTGATG
CACCATTTAAGAAAGAGAGAAAATAAAAATGCTCATTTCTAATTGTCCTCATTTCAGCAG
CTTCCCAAATATTCTTCTATTTCTTTCTTTTTAAGTAATTACCACATTTTCATATTTGCT
GAATCATGAA

The following amino acid sequence <SEQ ID NO. 174> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 40:

FMIQQIKCGNYLKRKKKNIWEAAEMRTIRNEHFYFLSFLNGASDAVFIALFFPNWNIFFLILLVYSLVTKK
VFRKYHNFPNSLLSAGDYEYILQNGKGGSSGPATICILKDLVELKSQRKWEELSKYFIIFFLEYQVLIHHI
FHHVSKSFFLKKVCIYISKRVSVVKKN

The following DNA sequence Seq-2396 <SEQ ID NO. 41> was identified in *H. sapiens*:

CCCGAGTGACAGAAGCCATTTCACTGCCAGAGACTCTTAGCGGCCTTCAGTTCTCTTGAG
CTGGAGCCACTGGGTCTTGTATGAAAGCTCACCAGGACATCTCATGTGGACCTCGGGCAT

CTGAGCCGGGACCATCCTATTACAAGTGCGGAAACCAGATCATTAATGCAGAGCTGAATT
CAAATTGTTACTTGCTAGCTTAGGAAAGAATCCTTGGAAATCCAACATATTGTCTAAATG
GATCAGTTAATCTTACTATGTGCATTCTACATACCCTTTCATTGTTTGGGCTTAAATAAC
TTTTCTGCTTTGTCTGGTTTAATTTCATCCAATGTGGATCGCTGGAAGAATATGATGTAT
GTTTTAGAATAGAAACAGTTCTGAGATGAAGTTGAGCACAATTTCCTGTTCTAGTTGCAA
TTAAATATAAATATAGCATTTGACATAAAATAGCTGGCCCGATATATTTAGAGTACAAGT
TAAGTGTCATCCCCTTAGAATTGGGCATTGACTCCGTAGAATTCCCCTTTGTACAAGGTG
AGCAAATGTATATTTTGTTAAAAATAAGTATCTGACTGCCAAAACGGACAGAAAGCTCTT
TGCCATATGTGTTTTCA

The following amino acid sequence <SEQ ID NO. 175> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 41:

ENTYGKELSVRFGSQILIFNKIYICSPCTKGNSTESMPNSKGMTLNLYSKYIGPAILCQMLYLYLIATRTG
NCAQLHLRTVSILKHTSYSSSDPHWMKLNQTKQKSYLSPNNERVCRMHIVRLTDPFRQYVGFPRILSASKQ
FEFSSALMIWFPHLDGPGSDARGPHEMSWAFIQDPVAPAQENRPLRVSGSEMASVTR

The following DNA sequence Seq-2397 SEQ ID NO. 42> was identified in *H. sapiens*:

CTTTTTAATTTTGTTTTTGTAGCAGTTGTTTGTATCCATGTGTGTTGGTGCCCATATGTA
TTGTTTGGGGTTTGGTTATTCTCTCAAAACCAAGTTACCGTAAAAAGTTTGAATTTTAGT
ATTTCTTTATTGAGTAGTGGGACCGTCTAGACTGTGTGCTGACTCTTACTAAAGTCATTT
GTTTTTCTTACCCGTGGAGAGGTGTATTCTTGAACCCTTTAAACGGGTCTCTACTTTGGC
CTAAGACCATATTAGAAAACTTTTTTGAAGTCACTTATTATATGCCATATAATTAAAAAG
TTATATGGTATATTCTCCCATTACATTTTAGCCACAATGCCCGTATATTAAATAAGCAAA
CAAACTATATGTGGCAATTAAAACTTAAAAAAAAAAGCCTGAATTGGCTCTTAGAAATAT
TTAATCAAGTAGTATCCACTAGAACTTAACATTTCATCCTGTGGATCATCACACACAAAA
TACCCAACCCTGCTGTCATTCAGGGTCCTAGCAGGAACAGGTAGCATCAAATAGGATAAT
TGATGAGAGCTTAAGAAAGGAACTATTTACAAATATGTGGCCAGATTAGGGGAAACCAGT
AAGGTTGGGAATGCCGCCCAGGATTCTAACAAGAGTGAGAATCTATTTCTACT

The following amino acid sequence <SEQ ID NO. 176> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 42:

LFNFVFVAVVCIHVCWCPYVLFGVWLFSQNQVTVKSLNFSISLLSSGTVTVCLLLKSFVFLTRGEVYSTLT
GLYFGLRPYKTFLKSLIICHIIKKLYGIFSHYILATMPVYISKQTICGNNLKKKAIGSKYLIKYPLELNIS
SCGSSHTKYPTLLSFRVLAGTGSIKDNELKKGTIYKYVARLGETSKVGNAAQDSNKSENLFL

The following DNA sequence Seq-2398 <SEQ ID NO. 43> was identified in *H. sapiens*:

TCCATGTAACATTGATGAGCACAGTTTTCTCTTCTGTAGCAAGCACTCCTCTGCCTAATT
CATATGACTAAAACAGTGCTTCTCAAACATATGGTCTCAGGAACCCTTTAAAATCTTAAC
AACTAGTAATGACCCCAAAAAGGTTTTTATAATATGAATTTTATATATAAATATTTTAT
TGGAAGTCCACTTTTATGAAAATAACCTTTTTTCAAAAATTTCATAAGAAAAAAATAGTA
TTATTTTACATATTTGAGGCATCTTTTTAATGCCTGGTTTAATAGAAGACAATTGAATAT
TCATGTCAACTTCTGGATTCGATCTGTTTCAATATGTGTCTTTGGTTGAAATACATGAAG
GAAACTTGGGATCATCAGACATATAGTTAGAAAAGGGTGGAGTATTTTAACAGCCTTTTT
GGACAACTGTGGACATTGTGCTTTGATATTACAACAAAACTGGAGAAGTGGTAGGTTCTA
AATGATTAGTTGCAACATGGAATCTGAAACCACATCATGAACTATTTGTAATCTGGCATA
TTAAGATCTATTTATCTATCTTGCACTTTGAATGGGATCCTTTGCTCATGCATCTTTTTG
TAACATGAATCATCTCAAACACGTTGGTTCATTGAGTTATGC

The following amino acid sequence <SEQ ID NO. 177> is the predicted amino acid sequence derived from

the DNA sequence of SEQ ID NO. 43:

HVTLMSTVFSSVASTPLPNSYDNSASQTYGLRNPLKSQLVMTPKRFFIIILYINILLEVHFYENNLFSKIS
EKNSIILHIGIFLMPGLIEDNIFMSTSGFDLFQYVSLVEIHEGNLGSSDILEKGGVFQPFWTTVDIVLYYN
KTGEVVGSKLVATWNLKPHHELFVIWHIKIYLSILHFEWDPLLMHLFVTIISNTLVHVM

The following DNA sequence Seq-2399 <SEQ ID NO. 44> was identified in *H. sapiens*:

AATTAAAATCCCTGCAGTCAAATTAGACTCTGCATGTCTGGGGATATTTAAAAGGATAAT
GTATAGGGGTTGCCATGGTAACTCATCAAGTGGTAATTCTGTACCTTTCTGAGTGAAAAC
CTTGAAAGGAGAAGACAAGCAATTTGGGGAGATAACAGCACCAGAAATTGAGTTCATCTG
TAACTTAGGCTCTCTGTGAGTTTGTTTACCAGCTATTCACCATGTGGATGAAAAACAGTA
AAAAGACAAAAAAGATTCACATTTCAAGGCTCCCTAAAATTGCCAATTCCACTCTATAGC
TGATTCTCAGCACAGGAGGAAATGGGACTAGAATGCTGGGAGATGACACTATCATCGAAC
AGTGAGCTCCAAGGAGAAGCCTAATTGTTACTTCTCAATGGCAGAAGGCGGGTGCTTCCC
CCGGGGCAGGATTCTGTTTAATCCTTAGGTTAGAGCCCAGCTTCAACCCAGTGTCACAGG
TCAATTACCACCCTCCAACCCTGAGGGGCGACATGAACCATACTCACGCACCGGCGCATG
CTCCCTCCTCAGCACCTCTTGTACATTCAGAGCTCCTGCATGGGATGCCGAGAACTCACA
CCCTTCCAGGGCTGCTGAAGATCATATGACTGATCATCAACTTTGATTTTTGACCCATCT
GTCAACAACGACAC

The following amino acid sequence <SEQ ID NO. 178> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 44:

IKIPAVKLDSACLGIFKRIMYRGCHGNSSSGNSVPFVKTLKGEDKQFGEITAPEIEFICNLGSLVCLPAIH
HVDEKQKDKKDSHFKAPNCQFHSIADSQHRRKWDNAGRHYHRTVSSKEKPNCYFSMAEGGCFPRGRILFNP
VRAQLQPSVTGQLPPSNPEGRHEPYSRTGACSLLSTSCTFRAPAWDAENSHPSRAAEDHMTDHQLFLTHLS
TTT

The following DNA sequence Seq-2400 <SEQ ID NO. 45> was identified in *H. sapiens*:

GCCTAACTGAATTATAACCGCGAGTTTGCACAGTGGTGAGCATAGCTGATGAGATGCAAG
CAAAAAAAGAGTATTGCTGACCTAGGACCATGAGGAAAAACCAAATCCAAATTAGTCAAG
TTGGAGGACATTTGTTGAAAACTCCACACTTCCATGAGGTCTGTAGCCTTGAGCCTATCA
GTGCCGACACAGAACATTCTGAATAGTTCAATGCCTCTTTCTGTTAAAGAGGAGACGCCT
CACTCTGCCGCTCAATCTTGGACTTGTTTGTGCACAGAGGTCCTTGCTTATGTAACACTC
GCTTTTAACTATAATTCACAGAGTCCTTTGAACACATAAAGGGAAAGCCACTTTCGCTCC
TGTTAAGGATGTATAAGCACAAAAAATGAACAGTGAATTAATCCTAGTGTTTTATACATT
TTTTTTTAAAAAAAGAATCTAAGCCAGAATGAGGTTACTGCCTAGGCAAAGAAGAAGACA
GCTCATCACAGGTGAGTGTAACACGTTTTTCATATGTACAAATTAAGCAGCCTGAAACAA
AAGGCACTCAAAAGGTAAAAGAATACCAGTCCACCCCTCTGATTTGTCAAATCAAAGTTC
TGTCAACTG

The following amino acid sequence <SEQ ID NO. 179> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 45:

SQNFDLTNQRGGLVFFYLLSAFCFRLLNLYIKTCYTHLAVFFFAAVTSFWLRFFFKKMYKTLGLIHCSFFV
LIHPQERKWLSLYVFKGLCELLKASVTARTSVHKQVQDAAEGVSSLTERGIELFRMFCVGTDRLKATDLME
VWSFQQMSSNLTNLDLVFPHGPRSAILFFCLHLISYAHHCANSRLFS

The following DNA sequence Seq-2401 <SEQ ID NO. 46> was identified in *H. sapiens*:

AAAAAAAAAAAAAATTCAGGGGAAAAAAGCAATTAAAAAAAACATAACTATAAAAATAATAC

AAATTACAAAACAACCATTTACATAGCATTTACATTATATTAGTTATAAGTAATCTAGAG
ATGATTAAAGTGTACGGAGGAATGTGCATAGGTTATATGCCAATACTGCCTCATTTTATA
TGAGGGACTTGAACATAGAAGGGTTTTGGAGTCCACAGAGGTCCTGAAACCAATTTCCCC
TTCCCATGCCTGGGATGACTGAATTATACAGCAGCAAAAATGAATATACTCAAGCTATAT
GCATGAGTCTCATAAATATAATGCTCACAGAAAAAAGCAAGTTGCAGAAGGGTAAATACG
GTTGATATATAAAGGTGCTAAACACAGAACTATTTAATGATATACGGATGCAGTAAAAGT
ATAAGAAATGTATGCAAACTTACTTAAATTCAGGGTGTTGGTTACTTGGAGTAAGGCGAA
TGTTTGGGATGTCAGTAGGTACCTGACAAATGGCAACTTAAC

The following amino acid sequence <SEQ ID NO. 180> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 46:

VAICQVPTDIPNIRLTPSNQHPEFKVCIHFLYFYCIRISLNSSVFSTFIYQPYLPFCNLLFSVSIIFMRLM
HIAVYSFLLLYNSVIPGMGRGNWFQDLCGLQNPSMFKSLINEAVLAYNLCTFLRTLSKCYVNGCFVICIIF
IVMFFLLFSPEFFFF

The following DNA sequence Seq-75 <SEQ ID NO. 47> was identified in *H. sapiens*:

AGCTAGGGTGGGCAGGAGTGGTCTCTGAGAGGTGACATTTGAGCTGAGACCTGAATGACA
AGAGACCAATGTCAGCTCTCTTTAAGAAAGTTTTCCTTTGTTTTAGTGGCTCTCTCCATA
CTCTTATTTTAAACTCACTTAACATCAATATAAAAGTGTCCTTTGCAGCAGGACACTTTT
AGGAGGTCTTGAGCCCCTCTCCCACCAGCACTCATCTGTGTACAAACAAGTTGTTGCTAG
TGGTGTTGGAGCTCGTTTTTCCCAAGCTTCACCTTGGCATTACCCAGATCTGTTCAACCC
TGGGCATCTCTTCCTCCCAGCTGGATGCTCACCCAACTTGTTCTGCCTCAGTTTCTGGAG
GAGCCTGACTCTATTTTTGCCCCCCTTGAAAGAAAGTACAGGACTGGGTTGAGGCAGCTG
CTCACACTCACCAGAGGCCTCCATATCTTGTAGGCCACACTGGCTGCCATCAAGAGCTGG
CAGTCCTGAGAAAGCAGAAAGCAGATGGTGAGGTAGAAGGAGCGAGTGATATGGAAGGGC
ACAAAACAGAGGGTGAAGAGGCCACACACCAGTAGGATGGTCCGGATGGACCTGGCTCGG
GCTGTGTTGCCTGTCCTCATGAGGTTCTCCTCTGGCTTGATCAGGCTCCTGACCATCAGT
GAATAGCACACCAAAGTGACC

The following amino acid sequence <SEQ ID NO. 181> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 47:

VTLVCYSLMVRSLIKPEENLMRTGNTARARSIRTILLVCGLFTLCFVPFHITRSFYLTICFLLSQDCQLLM
AASVAYKIWRPLVSVSSCLNPVLYFLSRGAKIESGSSRNGRTSWVSIQLGGRDAQGTDLGNAKVKLGKNEL
QHHQQLVCTQMSAGGRGAQDLLKVSCCKGHFYIDVKVNKSMERATKTKENFLKESHWSLVIQVSAQMSPLR
DHSCPP

The following DNA sequence Seq-76 SEQ ID NO. 48> was identified in *H. sapiens*:

CCAGGGGGAGGGGGGCACGGGCTATAAACGCTCGGCCGCAGCGGCGCCGGCAGAGAGCCG
CCGAGCCCAGCACAGCTGCCCTCTGGACCCTGCGGACCCCAGCCGAGCCCCTTCCTGAGT
TCCACAGGCGCAGCCCCCGGGCGGTCGGGCGGAGGGGTCCCCGGGGCGGTGCCAGGGCGC
AATCCTGGAGGGCGGCCGGGAGGAGGAGGTGCGCGCGGCCATGCACACCGTGGCTACGTC
CGGACCCAACGCGTCCTGGGGGGCACCGGCCAACGCCTCCGGCTGCCCGGGCTGTGGCGC
CAACGCCTCGGACGGCCCAGTCCCTTCGCCGCGGGCCGTGGACGCCTGGCTCGTGCCGCT
CTTCTTCGCGGCGCTGATGCTGCTGGGCCTGGTGGGGAACTCGCTGGTCATCTACGTCAT
CTGCCGCCACAAGCCGATGCGGACCGTGACCAACTTCTACATCGGTGAGTGCGGGCCGCT
GCGCCGCACCTGCTGCCGTCCCGGGGGGCTCCGAGGGCCGAGCGGCCTGGGGCGCCCTCT
CGCGACGC

The following amino acid sequence <SEQ ID NO. 182> is the predicted amino acid sequence derived from

the DNA sequence of SEQ ID NO. 48:

QGEGGTGYKRSAAAAPAESRRAQHSCPLDPADPSRAPSVPQAQPPGGRAEGSPGRCQGAILEGGREEEVRA
AMHTVATSGPNASWGAPANASGCPGCGANASDGPVPSPRAVDAWLVPLFFAALMLLGLVGNSLVIYVICRH
KPMRTVTNFYIGECGPLRRTCCRPGGLRGPSGLGRPLAT

The following DNA sequence Seq-77 <SEQ ID NO. 49> was identified in *H. sapiens*:

AAGTCGCCTGTCTTTGATCTGGTAGCCAGGCTGTGATGGCTAGCTTTAGGATATTTTCCC
TATATTTCTCTTGCTGTCAGGTTACCCCTTGGTATACCTGTAATTGATTTCCCCAGTTAG
AGAGTTTAGATGTGGACAGGGGAAGTACAAACTACAGCTTAGTGCAAGATAAACCAAGGG
TGTAATTATCAAGTTGTACTTGAACAGAAATATTACCCAATAGGATTTCCAAATGAACAG
GATGGCAAAGAGTTCTGGGGTGTGGAAGTCAGAGTAGGTGCCAAAGGATCTAGATCAAAG
GGGTTGGTAGATGAGCAGGGATGGGTCAGAGAAATCTAGGACTGTTAAAGCAAGCATGAC
CCAGGCCATGTTCTGAGGTTGGTAAAGTGAATTATAGAAGGTGAGACCAAATGTGAGATT
GTGAGATTTTAACCACCCCAAAGAGGGAGTATGTGCCTCAGGCAAAGAAAATGGGAAAAA
AAAAACATGGTATATGGCATATTTGAGGAGCAAAGATAAGTTCATTGTCACTAGGGCAGA
GCAAGGGATAAGTGAATGGTGTGAGACAAGATTGGAGAGGTTAACAGTGGCCAATAACAA
GTGATAAAAATAATTTCAAATGAGAGCAGCCCAGCACTTATAAAGTGGTTAATGTGCAC
CAAGTACTGCTTTAAGTTATCCTGCAGTATTATTG

The following amino acid sequence <SEQ ID NO. 183> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 49:

IILQDNLKQYLVHINHFISAGLLSFENYFYHLLLATVNLSNLVSHHSLIPCSALVTMNLSLLLKYAIYHVF
FFPFSLPEAHTPSLGWLKSHNLTFGLTFYNSLYQPQNMAWVMLALTVLDFSDPSLLIYQPLSRSFGTYSDF
HTPELFAILFIWKSYWVIFLFKYNLIITPLVYLALSCSLYFPCPHLNSLTGEINYRYTKGPDSKRNIGKIS
SPSQPGYQIKDRRL

The following DNA sequence Seq-78 <SEQ ID NO. 50> was identified in *H. sapiens*:

GCCTCCAACCGATATTTCTGTCTGTTGCTCTGACCAGGTACTGGGCCATCACCAATGCCC
TGTAGTATAGTAAATGGGCCATCTCAAATTGTATCTCTATCCCAGTGCTCTTCTCCTAGA
CCTCTTGCACCACCTACTCCACATGTAAGACCTTCTACATTTTGGTTGTGTTGTTCATCA
TCTTCACACATTGCCCAACAAGAACATCCAGAAGCCATCATCACAGCACCACTGCCCAGG
TCATCACAGCTCACTCTTCTTCCTCAACCCCAGCCTCCATGAGAGGCAAAGGCGCTTAAC
TGGCTCTCCTCTGCTTGTTAATCACATGAAAATCAAGCATGCTTATAGTGTCCTAGTACA
ACAGGAAATTTACTTTCAAACAAGGAAAGCCACAGAAACCCTGGGGATCATTTTAGGGGC
TTTTATCATCTGCTGGCTGCCTCTCTTTATTGTTTCTCTGCCAGCCAAGATACCACCATA
TTAAGACATCTTCATCTTGCTGAGCTTTTTTTTTTTTTTCTTTTTGATACCAAGTCTCAC
TCTTGTCTCCCAGGCTAGAATGCAATGGTACAATCTCAGCTCACTG

The following amino acid sequence <SEQ ID NO. 184> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 50:

PPTDISVCCSDQVLGHHQCPVVMGHLKLYLYPSALLLDLLHHLLHMDLLHFGCVVHHLHTLPNKNIQKPSS
QHHCPGHHSSLFFLNPSLHERQRRLTGSPLLVNHMKIKHAYSVLVQQEIYFQTRKATETLGIILGAFIICW
LPLFIVSLPAKIPPYDIFILLSFFFFFLIPSLTLVSQARMQWYNLSSL

The following DNA sequence Seq-79 <SEQ ID NO. 51> was identified in *H. sapiens*:

CAGGCGCCTCAACTGTTCCACAAACCAAGCCTGAAACCAGAACTCCAACTTCTAGTCTGA
AAAGCAAAGTGGCACCTCGCAAACACCCTGTGGCCCCAAGTAGTCTCACCCAACCTTGGG
GAAGAAGCAGAATTCAAGCTGTAACTGCCTGTTGGAGAGAGCCAACCCTCGGCCTCTGTC

CTCGAAAGGCAGCACCAAAGTTTTCCAAGTGGAATCAAATGTGCAGGGAGGATC

The following amino acid sequence <SEQ ID NO. 185> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 51:

ILPAHLIPLGKLWCCLSRTEAEGWLSPTGSYSLNSASSPRLGETTWGHRVFARCHFAFQTRSWSSGFRLGL
WNSGA

The following DNA sequence Seq-80 <SEQ ID NO. 52> was identified in *H. sapiens*:

CTGTACCTGTCACAGTTATCAAAAATTTATTCATTCAGAAGTCTTTGTTGAACACCTGTT
ACGTGTACTGAGCATTGTCCTAGGTATTTGAGATACATCAGTGAACAGAGGATCCTTAAC
AGACAATATACATAATAAGTTATGTAATAGCTTACAAAGTGACAGTACCTTTGGGAAAAA
GGAAAGGTATTATAGGATAAAGATGATCAATGAACAGGAAGTTTGCAGTTTTAAATTGAG
TGGTCTGGGTAAGGAAGATCATACCTGAACCAAGACACAAAGGAGGTTAGGGAATGATGA
GCCCTGCA

The following amino acid sequence <SEQ ID NO. 186> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 52:

CRAHHSLTSFVSWFRYDLPYPDHSINCKLPVHSSLSYNTFPFSQRYCHFVSYYITYYVYCLLRILCSLMYL
KYLGQCSVHVTGVQQRLLNEIFDNCDRY

The following DNA sequence Seq-81 <SEQ ID NO. 53> was identified in *H. sapiens*:

TAGCAGAGCAGGTGCTAGTGATATTTGCAGAACAGGTGCTGAATGAATGCATGAACAAAT
GCATGAATGTGGAAATGAAAGGGGATGCAGATGGAGATGATGCAGATGGAGATGATGATG
CAGATGGAGATGATGCAGATGGAGATGATGCAGATGGAGAGCAGTGGCCATGCAGAGTCT
TTGCAGACCTTGGCTTGGCTTCAGGCTGTGGGGGCTCTGCAAGCCAAGGGTTTGAGTTCC
ACCTCCAGTGCTTGCCAGCAATGCCACCTTGGGTGACCTTTATCTTGCTACCTGGAAAGT
GGGGATGCTGGCAGCCCCTCCCTCCTGGCATCACTGACACTGCATGGTCAGGGTGTGATC
CCTTTGGGTACAGGCGGGGGTGGTGGACCTCCCAGGTGGGCAGGTCCAGTTTGGATGAAA
GGCCAAGGACGATTCATAGGAGAGCACAGGAGTCCTTGCTTAGCCCCAGCAATTCCACAG
AACCTGCTGTGAACTGCTGGCTGCTGCCCGTAACTTTTCCCTGTCCCTATTTCCACTCCT
TGGAGGCCGCAAGAACAACTGCTGGCTGGCCTTGGCCACTGCCT

The following amino acid sequence <SEQ ID NO. 187> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 53:

AEQVLVIFAEQVLNECMNKCMNVEMKGDADGDDADGDDDADGDDADGDDADGEQWPCRVFADLGLASGCGG
SASQGFEFHLQCLPAMPPWVTFILLPGKWGCWQPLPPGITDTAWSGCDPFGYRRGWWTSQVGRSSLDERPR
TIHRRAQESLLSPSNSTEPAVNCWLLPVTFPCPYFHSLEAARTTAGWPWPLP

The following DNA sequence Seq-82 <SEQ ID NO. 54> was identified in *H. sapiens*:

AGTCTTTTTCTTTAGGGAACTTTGTTGTTGCTTCACTATATAGTTGTTGTTTCAACAATT
TTGTGTTGTTTCACAGTTTCACTGTGACAGTTTGATGTTAGGTTGATTCTTTTTCCTCCT
CTGTATAAAAGATTATGTCACCAGAATCTTCTTTCATTACTTTGGATAGGACCTAAAGGA
CCCTCTCAATCTGAAAATCTATGCTATTTGTTATCACAGAGCAGTTTTCTGCTGTCATTT
CTTTGATTGTTACTTTTCTATTTATTCCTTTTTCTCTTTCTAAAATGCCATTATTTGTAT
ATTGGAGTCATAGATCTGAGATCTGTGAATTTGCTATTCATGTCTCATATCTTTTTGCAA
ATGGTTTCCATGTCTCCAAGTCTTTGTTCTCTATTGTGAGATATTATTTGTATTGTTTTG
TCCAGAATATTAATTTAGTTCTATTCATTGACTATTCTTTGGTTTTGCTGTTGAATTTTT

AAATTCAGGAATAGTGTGTTTTTCTTTCAGATTATTTTTTCTGTGACCTAATTGCATCT
TCTTACGGGGTCTTATTATA

The following amino acid sequence <SEQ ID NO. 188> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 54:

SFSLGNFVVASLYSCCFNNFVLFHSFTVTVCVDSFSSSVKIMSPESSFITLDRTRTLSIKSMLFVITEQFS
AVISLIVTFLFIPFSLSKMPLFVYWSHRSEICEFAIHVSYLFANGFHVSKSLFSIVRYYLYCFVQNINLVL
FIDYSLVLLLNFIQECVFLSDYFFLPNCIFLRGLII

The following DNA sequence Seq-83 <SEQ ID NO. 55> was identified in *H. sapiens*:

GCCCAGGGAAGCCAAAAGATTGGACATCCATGCTCCCCTCCTCTCCCTTCCCGACTGCCA
TCTCTTGATGGCGGCCAGTGTGGCCTACAAGATATGGAGGCCTCTGGGGAGTGTGAGCAA
CTGCCTAAACCCACTCCTGTACTTTCTTTCAAGGGGGGCAAAATTTGAGTCAGGCTCCTC
CAGAAACTGAGGCAGAACAAGTTGGGTGAGCATCCAGCTGGGAGGAAGAGATGC

The following amino acid sequence <SEQ ID NO. 189> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 55:

PREAKRLDIHAPLLSLPDCHLLMAASVAYKIWRPLGSVSNCLNPLLYFLSRGAKFESGSSRNGRTSWVSIQ
LGGRD

The following DNA sequence Seq-84 <SEQ ID NO. 56> was identified in *H. sapiens*:

TCCTTGGTCATTTTGGTGTGCTATTCACTGATGGTCAGGAGCCTGATCAAGCCAGAGGAG
TAACCTCATGAGGTACAGGCAACACAGCCCGAGCCAGGTCCATCCGGGACCATCCTACTG
GTGTGTGGCCTCTTCACCCTCTGTTTTGTGCCCTTCCATATCACTCGCTCCTTCTACCTC
ACCATCTGCTTTCTGCTTTCTCAGGACTGCCAGCTCTTGATGGCAGCCAGTGTGGCCTAC
AAGATATGGAGGCCTCTGGTGAGTGTGAGCAGCTGCCTCAACCCAGTCCTGTACTTTCTT
TCAAGGGGGGCAAAAATAGAGTCAGGCTCCTCCAGAAACTGAGGCAGAACAAGTTGGGTG
AGCATCCAGCTGGGAGGAAGAGATGCCCAGGGTTGAACAGATCTGGGTAATGCCAAGGTG
AAGCTTGGGAAAAACGAGCTCCAACACCACTAGCAACAACTTGTTTGTACACAGATGAGT
GCTGGTGGGAGAGGGGCTCAAGACCTCCTAAAAGTGTCCTGCTGCAAAGGACACTTTTAT
ATTGATGTTAAGTGAGTTTAAAATAAGAGTATGGAGAGAGCCACT

The following amino acid sequence <SEQ ID NO. 190> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 56:

SLVILVCYSLMVRSLIKPEEPHEVQATQPEPGPSGTILLVCGLFTLCFVPFHITRSFYLTICFLLSQDCQL
LMAASVAYKIWRPLVSVSSCLNPVLYFLSRGAKIESGSSRNGRTSWVSIQLGGRDAQGTDLGNAKVKLGKN
ELQHHQQLVCTQMSAGGRGAQDLLKVSCCKGHFYIDVKVNKSMERAT

The following DNA sequence Seq-85 <SEQ ID NO. 57> was identified in *H. sapiens*:

GTCACACTGAATTAGGGACCACCCTTGTAACTCCATTTTAACTCGATTGTCTCTGTAAAG
GCCCAGTCTCCAAGTACAGTCACATTCTGAGGTACTGAGGGTTAGGACTCCAATGTATCT
TTTTGAGGGGACACAATTTAACCCTAATAGACCACAATTAAAATGGAATGCAATAATAAA
AACTAACTTTTATTGAGCATTCGTAGTCTGAGTTTGGCATTGCTCAAGAGTGCCTTACAT
TAATTAATGTAATCTTCACAATCCTATGAACTCAGTATCATTATTACCCACATCTTACAA
ATGAGTGGTTGGAGTCCATGGCAAGAGTAACTTGCCCAAGGTCACGCTGCTGGTAAGATC
AGAACCAGACTCAAAAACAGTAGTCTAATTCCACAGCAGATTCCGTCAACAACTATTCTA
CACAGTCTCTACTTTATGGGGTTCAACATAGAGACTATTTTGATGTCTGCGGTAGCTGTG

AGAATGTGGCTCAGAGACTTCCATCTATGGGGAACTCAATCAACCAAAGGCCCCAGCTCC
TGCACTTTGAGACCTGTCACTATGTTATCACCGAGCCCACATTTCCCATGGGCTGCTTCC
AGCCAATGCCCAAACAATGGCAGGGAGACTAAGGCATCCTGTTCCTGGGGAGATGTGGGA

The following amino acid sequence <SEQ ID NO. 191> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 57:

SHISPGTGCLSLPAIVWALAGSSPWEMWARHSDRSQSAGAGAFGLSSPMEVSEPHSHSYRRHQNSLYVEPH
KVETVNSCRNLLWNTTVFESGSDLTSSVTLGKLLLPWTPTTHLDVGNNDTEFIGLRLHLMGTLEQCQTQTT
NAQKLVFIIAFHFNCGLLGLNCVPSKRYIGVLTLSTSECDCTWRLGLYRDNRVKMELQGWSLIQCD

The following DNA sequence Seq-2337 SEQ ID NO. 58> was identified in *H. sapiens*:

ATTCTGTCCTCTTCTCTCTGCCTGCGGCCCCCATCTCCTGAGCCCAGCGAGCTCAGTGCT
AGTTCACTGTTTGCTCCTCCTTGCTGCAGACACAGAAGATTTGGGAGCGTTCCTGCCGAG
GTTGGTAAGGATACCTGGAACAGTGGGCGGCCTCTTTGCTCCCCACTTGCTAGGAGTAAA
GCCGTTTAAAAAGACACCTGAGCCTCTCCGGGTTCCTGCTCCTCACTCAACCCCACAGTA
GATCTGGTGGGGAGGTTGAGGGCTCAGTGAATCTGCAGGTGCAGCATCGTGTCCTCAGTG
TCCTGCCCCCTGCTTCCACCCGGTGTCGACAGCTGCACGGTCCACCCCACGCCTGCCTTT
CCATCGTTCCTCATCAGCCCTGTGATCTTTCCTGTGGCCCTGCTGTGCTGGTGCCCTGTG
AGGTCCTGTGGACACAAGAGACTGCACGGGCCACACCCCCAGCTGGGTGAGTCCTCTCCC
TCCTGGGTACTCTGGACAGTAAAGAAAGATGGACACGTGGGCTCCGTGGAGCATGAGGTA
GTCCAGGACCTCGGCGGCCACAGGTCCTGCCTCCCTGCTTCTCGTGCCCTCCCTCCCTTT
GGGTCTCTGCTCCACCTCGGTAAACGCTTCGTTCCCACCCCTC

The following amino acid sequence <SEQ ID NO. 192> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 58:

ILSSSLCLRPPSPEPSELSASSLFAPPCCRHRRFGSVPAEVGKDTWNSGRPLCSPLARSKAVKDTASPGSC
SSLNPTVDLVGRLRAQICRCSIVSSVSCPLLPPGVDSCTVHPTPAFPSFLISPVIFPVALLCWCPVRSCGH
KRLHGPHPQLGESSPSWVLWTVKKDGHVGSVEHEVVQDLGGHRSCLPASRALPPFGSLLHLGKRFVPTP

The following DNA sequence Seq-2338 <SEQ ID NO. 59> was identified in *H. sapiens*:

AATATGTCTTAATATTCTAGTAGGGTTAATTCTTTATTGCTTTTTTCTTTCTAGAATTTT
TCTTATATTATTTTTCATATAAATTTAGAATAAGTCTGGTTTGGGGGTCATATAGCAA
TAGGTAAATTGATTAATAAAGTGATTTGGTGAAGGTTTCACAATACATTTATGAATCAAC
TTCGGGAGAGTGGTTATGCTTATGTTTAGTCATTATATTTTAAAATGTGACATATCTTTC
CATTTGTTTTAAGTCCTTGATCAAGCATTAGTTGCCTCCTCTGAGAATCTATAATTAAAT
TCAAGATAAAATAATTTTTTCCATTTATTGACCCATTTTTAGCTTACAATTTGTTTTCTA
CCCTTGTAAGTATTATGTTTGGTAAATTATTTTTTATTAATATCTCCCTTACAGATATTA
TACGCCATAAGGAAAGGAGTCACAGATTTGGTAATAGAGACTCAATACACGTTTGTTGGA
ATGATGAAAGCATTATGAGGCATATTTTCTTACTATGTTCACCTAATAATCTTAAAGTTA
TCAAGTTATTAAGTAGAGCCCATTCACAAGTCCAGATCTTTTGATTTTAAATCCTGTATT
TTTCCATATTTTCAATATTTAATAGGGGAAGTAACATGCTAAAATGCTATAGTTTTGCAA
TTTTATATCT

The following amino acid sequence <SEQ ID NO. 193> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 59:

NMSYSSRVNSLLLFSFNFSYIIFHINFRISLVWGVIQVNLIKFGEGFTIHLINFGRVVMLMFSHYILKCDI
SFHLFVLDQALVASSENLLNSRNNFFHLLTHFLTICFLPLVLCLVNYFLLISPLQILYAIRKGVTDLVIET
QYTFVGMMKALGIFSYYVHLIILKLSSYVEPIHKSRSFDFKSCIFPYFQYLIGEVTCNAIVLQFYI

The following DNA sequence Seq-2339 <SEQ ID NO. 60> was identified in *H. sapiens*:

AAGGAAAATGGAAACTAGATGAACGTGACAATATAAGACTTCCAAATCCACGTGGTTCCA
TGAAAATAGGAAAAACCGAATGCCAAAGGGCAGGCCACAGAAGGAGGAAGACCAGCGCTA
TGAGCAGGATGGTCACGTACAGCCTGGTCAGTGGCATCTTCCGGGACCCACAAAGGATCC
TGACCAGCAGGACCAGGCTGGAACCACAGAGAGCCACACATAAAAAAATCAGCCCCCCTA
CTATGATGAAATCTGATGTTTAACACCAAACAGAATCAGCACCACTAAACAGGAAGTCAC
AGAAACTCCACTCCAGGACGCTCCGCAGCAGAGACAGGGCCCAGAGCATGACACACACGA
CCGCTGACAGGTGTAGGGGCGGGGGCGGCAGCGCTACCAGATGGGCCACAGGACGTACAG
GCAGCGCTCGGTGCTCATGGCGCTTAGAAAGCTCAGGCTTGCAAGGTAGGAAAACATCAT
CACAGGGCTGAGGATTTTGAAGATGGATGGAGGATATTGATGAGGCTTAACGGAAAACG
TATAATGTGGCTTCTGAGAAAGAGGAAGTCGGCCATGGACAGGTTGAAGATGTAGATGGA
GAAAGCGTTCCTGCGCATGCGGAAGCCCAGGAGCCAGAGCACGACTGCATTTCCTGTCAT
CC

The following amino acid sequence <SEQ ID NO. 194> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 60:

MTGNAVVLWLLGFRMRRNAFSIYIFNLSMADFLFLRSHIIRFPLSLINILHPIFKILSPVMMFSYLASLSF
LSAMSTERCLYVLWPIWRCRPRPYTCQRSCVSCSGPCLCCGASWSGVSVTSCLVVLILFGVKHQISSGGFF
YVWLSVVPAWSCWSGSFVGPGRCHPGCTPSCSRWSSSFCGLPFGIRFFLFSWNHVDLEVLYCHVHLVSIFL

The following DNA sequence Seq-2340 <SEQ ID NO. 61> was identified in *H. sapiens*:

CACACACACACACACACACACACACACACACACACACACACACACGCACGCACCCCATTA
ATGGGTTCCCTGGGGGCAGGGCATCAGTCCCACTCACTGCTGGGCCTCCAGGGCCTGCCA
AAGGGGCAAAGTCACACTCAGACATAAACTCTTGGTTTTAGCAATCCAATAAACAGTCAT
GAAACTAAGTGAGGAAAGTTATTAGATTGAAGGGATTTGAGGGAAAGTCCCATCAAAAAG
TAAAACTTGATCCCACCTCCACTTCTTGGATGAGTTACTTAATCTCTCTGGCCTCAGTTT
TTTCACCTATAAAATAGAAACCATGAGAGGACCTACCTCACCAGGCTGTTCTAAAGTTAA
ATGAGTTAATTCCTGTACAAGCTGAGAACAGCATCTGATACAGTATCTAATAAAGTCAGT
TATTATTACTTTTATTATTATTATGTACTTGGTTATCATTATTTTCATTCATCAATTATT
ATTCTCTTCACCTCTTTGCTGCCACCTGGAGTTCCTGGAACCCCTTCACGGCGTACAGCA
GGGAGACAGGGGAGGGCAGATGCCATTTGCACAGCCATTGGGACTAATAAGCCCCAGCAC
CCC

The following amino acid sequence <SEQ ID NO. 195> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 61:

HTHTHTHTHTHTHTRTHPINGFPGGRASVPLTAGPPGPAKGAKSHSDINSWFQSNKQSNVRKVIRLKGFEG
KSHQKVKLDPTSTSWMSYLISLASVFSPIKKPEDLPHQAVLKLNELIPVQAENSIYSISQLLLLLLLLCTW
LSLFSFINYYSLHLFAATWSSWNPFTAYSRETGEGRCHLHSHWDAPAP

The following DNA sequence Seq-2341 <SEQ ID NO. 62> was identified in *H. sapiens*:

TAATGTGGGACTAAAAAACTATTAAAAAATAATGACTTCAACCTTCCCAAATTAGGATGG
AAGAACATAAACCTAAATATTCAAGGAAACAGGAGCAAACCCTAAATAGAATACACCCAA
ATACATTCAATTTCTGGAAATGAAAAAAAAAAATTAAAAATCTTGAAAGCAAACAGAGGA
AAAATGGCACATTTCTTACAGAAAAACAATAATGTAAACCACAGCAGATTTTCCATCTGA
AACCATGAAGGTTGGAAGGAAACAGATAATATTTTTGAAGTACTGAAAGAACAGAACTGT
GAACTGTAAATTCAATACCCAGCAATAATATTCTTCAGGCACTAAAGTGACATAGAAAAC
ATTGTCTAATGAAAGAATGCTAAGGTAATGTGTTGCTAACAAACTTACCTTTAAAGAATA

AGTTCTC

The following amino acid sequence <SEQ ID NO. 196> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 62:

ENLFFKGKFVSNTLPHSFIRQCFLCHFSARILLLGIEFTVHSSVLSVLQKYYLFPSNLHGFRWKICCGLHY
CFSVRNVPFFLCLLSRFLIFFFHFQKLNVFGCILFRVCSCFLEYLGLCSSILIWEGSHYFLIVFSHI

The following DNA sequence Seq-2342 <SEQ ID NO. 63> was identified in *H. sapiens*:

ACCTCTAACTTTCTTCACTAATGTGTTGATGTCTGTCACTGCTTAACAAGCAAAATGGCA
TCAGAAAGAGGGTGAACAAATAAAGGTATATTTAGGGCTAATGATGAATTCGAGGTAAAG
CACATCAATGTTTCCACCAAGGTTTTTGCTTCCAGTGTGGTAGGGCAAAAAGATGTGAAC
TGAATTATTGGTACTCTCAAATTAAATGTATTCATTTTATTAATTCATTTAGCAACAGAC
ATACACAGGTACATATACCCATATCCGTAGTTTCACTTATAAAGAAAAATTAAATCCACC
CAACTGTTTTGTTTTCTGCAATATTTTTAACTTCTGTGACTTTTTGTTTTTTCCATTGCT
TTGAATCCACAATAGGTAGGTAGGAGAATTTGAAGCACCATTGAAATGAAGTATTCTAGA
AAAGTATGCAGAAAGATAAAGAAAATGCATCCATCTCTAGAAGTGCTTACATCTACTTAG
CAAGTGTGAAACTCACAATGAGGATTTAGCCTGTTAGTATGGCACAGATTATAAATAGGA
GAGTCGCTGT

The following amino acid sequence <SEQ ID NO. 197> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 63:

SDSPIYNLCHTNRLNPHCEFHTCVDVSTSRDGCIFFIFLHTFLEYFISMVLQILLPTYCGFKAMEKTKSHR
SKYCRKQNSWVDLIFLYKNYGYGYMYLCMSVAKINKMNTFNLRVPIIQFTSFCPTTLEAKTLVETLMCFTS
NSSLALNIPLFVHPLSDAILLVKQQTSTHRKLE

The following DNA sequence Seq-2343 <SEQ ID NO. 64> was identified in *H. sapiens*:

ACCTTGGCCTCCCAAAGTGCGGGGATTACAGGCGTGAGCCACCGCGCCCGGCCTAATTTT
GTATTTCTTATTCTGTATTCTTTTCCTTAAAAAACCTTTTGCCCAAATTGTATCAACTTC
AATACCCCAACGCTGGACCCCTCCCTAGATACAGTCATAAAGCAAATGACACGTTAGACC
ACGTGCTCCGCTAAGAACATAGAACCTCTGGCCTGGGTGATACTTGGTGTTTCTGAAGAA
GCTTTTCCTGGGGTGGAGGAGGAGGAGGAGGAGGAGGAAGACCCTTTGAGCTTTAAAATG
CCCAGGAGCCATTTCCTGTAATGGGTGGATGCAAAGAAGTAAATGATGGGGTAATGCCAC
AGTTCATGTTCATGAGGGCCACGGTGGCCTGAAGGGACAGTAAGAAAGCCCTCCGCTCGG
CACAGGATGGCAGGTGGAGCATACCTCTCGCCATGAACTGCTTGATGTTGAGGTGGTAGG
GGCTGAAGCAGACCACCACGGCCACCAGCATCAGCAGCGTAAGCAGGCAGCCTCGCCAGT
GGCGTCCTTTCCTGCT

The following amino acid sequence <SEQ ID NO. 198> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 64:

SRKGRHWRGCLLTLLMLVAVVVCFSPYHLNIKQFMARGMLHLPSCAERRAFLLSLQATVALMNMNCGITPS
FTSLHPPITGNGSWAFSSKGLPPPPPPPPQEKLLQKHQVSPRPEVLCSRSTWSNVSFALLYLGRGPALGY
SYNLGKRFFKEKNTEEIQNAGRGGSRLSPHFGRPR

The following DNA sequence Seq-2344 <SEQ ID NO. 65> was identified in *H. sapiens*:

CATACCCACTGAGGGAGAATGGAGAAGAGGGTGGGGTTCTGCTTGCAGGGCCCTTTGCAC
TTCAAATATTTTACAGGGAAGGGGATGGCAGATGCACCCTCTGCCAAGGGAAGCTTTGAG
GGCCAGCATCACATAGCCCTGTGGTGAATGAGAGCTGGCAGGGTGACAGTCTGCGAGGAA

GGAAGGATGGAGCTCCGACCCCTTTGCTTTCTGAAACTCCTGCTGAGAGAGTTGGCTCCA
CAGCCCTGGTAGGGCTCGGGTAGCTGCTGTGGCTGAATCAGTCCTCTGTTATCACCCGCT
CGGTGCCATGAAGTGGAAAAGCAGTCTCTGCCCTCCTCGTTCCTCCAATAAGCCCATCCT
AATCACCCTTATCATGCTCCTTCCACACCCTGAGAAAAAATGGCCTCGCAGCAGACGTTT
GAAGTCACCGGGACTGGAAAAGTCTTTCAAATGGCACCTGATTTGGCTACATGCCTGCAG
ACAGGTGAAAGTTAGTGCCCCCATTTCACAGGTGAGGCCACTGAGGTTCAGAGAAGTCAA
TCAATGATGTGATCATGCTCACACATCCCAGCAGTGACCAAATATGTAACATTCATACAC

The following amino acid sequence <SEQ ID NO. 199> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 65:

VYECYIFGHCWDVASHHLTSLNLSGLTCEMGALTFTCLQACSQIRCHLKDFSSPGDFKRLLRGHFFSGCGR
SMIRVIRMGLLEERGGQRLLFHFMAPSGQRTDSATAATRALPGLWSQLSQQEFQKAKGSELHPSFLADCHP
ASSHSPQGYVMLALKASLGRGCICHPLPCKIFEVQRALQAEPHPLLHSPSVGMHSPSVGM

The following DNA sequence Seq-2345 <SEQ ID NO. 66> was identified in *H. sapiens*:

CCTGCCCCCACCACCAATACTGGTGCCCACGTAAGTTGTCTAGTGAACTGAGGAAATATT
CTCCTCATCAACTGCCACTCTCAAGGGCCCAAGTGTACCATTTGGAGGCTTAGGTATTGA
TCTGCCCCACCGGTCATCACTGGCACCCATGCACACCTTCAGGGACCTAAGGACAGGCCC
ACTCTGCCTGCCACTGTCATTACTGGTACGCAAGGACTGGCCTGCCTAGTGTCTCCATCC
ACAGCAAAGCATTGCCACAGCCCCTAGTTGTTAAGCCACTGAGGAGCTCACAGACACCAC
TCACACTGTTTACAGCAGGAGAAATCCTATGGGGCCTATAATACTGTGCCCACCTTGGAT
CAAAACCAAAGTACTCTATGCAACTAACACTACAGCTATATCTACAGGAAAAAGCCTCTC
CCTACAAAAGCCAATCCAAAAACCTAGGAGAAGCAACTGTCACACCAAATACACAGATAC
CAACTTAAGAACATAAGAAACATGAGAAAACAAGGAAACATGGCATTTTCTAAAGGAGCA
CAATAACTC

The following amino acid sequence <SEQ ID NO. 200> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 66:

LPPPPILVPTVVTEEIFSSSTATLKGPSVPFGGLGIDLPHRSSLAPMHTFRDLRTGPLCLPLSLLVRKDWP
ACLHPQQSIATAPSCATEELTDTTHTVYSRRNPMGPIILCPPWIKTKVLYATNTTAISTGKSLSLQKPIQK
PRRSNCHTKYTDTNLRTETENKETWHFLKEHNN

The following DNA sequence Seq-2402 <SEQ ID NO. 67> was identified in *H. sapiens*:

AGCTGGGATTTCTGCTAACTGATGTCCAGTCGGTATTTGGATATCTCCAATGACATGAAA
CTCACTACTGCTCAGCAACCATAGGAAGACACTGGCCAGCCCATCCACTCATGCGGTGCT
GGAACCCTTTTTTTATTTTAAAATATTTAATTGACAAAAATTGCGTCTGTTCAAGGTGCG
ATGTGATGCTTCGATCTAGATATATATACAGGTATATTGATTACCACAGTCAAATTAACTAA
CAAATCTATCACCACCCATGATTACCATCATGTTGAGGGGATGAGGCAGTGAAGACACTA
AAGATCTGCTGTCTTATCAAATTTCAAGTCAACAATACAGTATTATTAACACAGTCACCA
TGCTGTGCATTAGGTCCCCAGAACATGTAACTGAAGGTTTGTATCTTTTGACCAACATCT
CCCCAGCTCTGCATGAGTGGATGGTCAGCATTTTCCAAACCCACTCTGAAGACTTTGCCT
GGTTGGCTACATCAATATCTCCTGAGAAAGTACAAAAGTCCAGGCCCAGTCACAGAAATT
CTGATGCATA

The following amino acid sequence <SEQ ID NO. 201> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 67:

LGFLLTDVQSVFGYLQHETHYCSATIGRHWPAHPLMRCWNPFFILKYLIDKNCVCSRCDVMLRSRYIQVYL
PQSNLTNLSPPMITIMLRGGSEDTKDLLSYQISSQQYSIINTVTMLCIRSPEHVTEGLYLLTNISPALHEW
MVSIFQTHSEDFAWLATSISPEKVQKSRPSHRNSDA

The following DNA sequence Seq-2403 SEQ ID NO. 68> was identified in *H. sapiens*:

CAAAATATACATGCATGTACATACTATGAAATATGTATTATGTAATTTTTGTGATTCTAT
GTATAAGTTAAATGCTTTTATATTTGCATTTTAAATTGATACTGCACAACATAAAAATGA
ATGTGAAAATTTATTGTGGTAATTTAGATTTTTAATTTTTTTACATAAAAGGACATAGAA
TAGCAAAGGAAAAACAAAACAAACAAACTGAAAGACGTAACAAGTTGAAAAATAGATCAC
AGATAAAGGAAACATTTTATACTTTGATACACTTAATAGAACCTTTTGCTTATATTTTGA
ACTAGAGCCCCACACTTTCATTTTGCACTAGACCTTACAAATTATATAATCAACCCTGGA
CACTGAATTAAGACAAAAGCCAATATTTACAAAAATGGGCACCATAGCCCAAGCTATTGC
TTTGAAGCTACATTAGTTCCTGTTTCCAGCTGTGAGCCTGAACTCCATTTTAGGAAGTGA
GACTGGCCAGGGTTTCTGTGTAGAGTTTGGCATTTTTATTCTCTAGGACCCTGCAAGAGT
CTACAGTAATTGTAGACTCAAAAATGTCAGAGATTGCTGCTTGTATTTATATAATGCCCC
ATACT

The following amino acid sequence <SEQ ID NO. 202> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 68:

YGALYKYKQQSLTFLSLQLLTLAGSRIKMPNSTQKPWPVSLPKMEFRLTAGNRNCSFKAIAWAMVPIFVNI
GFCLNSVSRVDYIICKVCKMKVWGSSSKYKQKVLLSVSKYKMFPLSVIYFSTCYVFQFVCFVFPLLFYVLL
CKKIKNLNYHNKFSHSFLCCAVSINANIKAFNLYIESQKLHNTYFIVCTCMYIL

The following DNA sequence Seq-2404 <SEQ ID NO. 69> was identified in *H. sapiens*:

TATTTTCCTATCTACCACATGGAATCAGAACTGTCTTGGAGATTTATGCATCTGAACAAT
AATATTTAGAACATCATCTCGTCTTTGACACCACTTTGTTCAACACAAAATGGCTATTCA
AACTACTCTGGAACCCTGTCTTGTCAACCAATGCAGGAATCTTAGTTAATGTATTCCATA
AACACACGCAGGTTTCCCTTAAGCACAGACTCCATGTAAGACAAGTTTCATACTTTTTCA
TTGTGAAAGATGCAGGTACTATTGGATGGATCTGAAGAGTTGGCAAAATGACAGGAAGAT
CAGGCAGGCTGCCTGTTTTTAACTTTATGAAATTTTTCATGTTTTATTATCTATCTACTC
AGATAAAATTAGGTGGGACACATTTTTAATGCTTCCAATAAATAAGAAAAATGTGCCTGC
AGCATGAAAAATCCTTTGACTGCCTTGTGTTATTTGCAACAGATGAATCTAATTTGTATT
CAGACATCAGTGCTATAACTAACTAGAGAAATAAAATGGATGTCTATGATCTCTCTTCAA
TTATTTAGTAAGGATGAAGTGTCAATTGGCTAAAAGTAATAACACCATGGCTGTACTTAG
TGTTACACCTATTAGGTAGAAATATACACACATACACGCATATATACAACAGATTAATAA
CACCAGAAG

The following amino acid sequence <SEQ ID NO. 203> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 69:

SGVINLLYICVYVCIFLPNRCNTKYSHGVITFSQLTLHPYIIEERSTSILFLLVIALMSEYKLDSSVANNT
RQSKDFSCCRHIFLIYWKHKCVPPNFIVDRNMKNFIKLKTGSLPDLPVILPTLQIHPIVPASFTMKKYETC
LTWSLCLRETCVCLWNTLTKIPALVDKTGFQSSLNSHFVLNKVVSKTRCSKYYCSDAISKTVLIPCGREN

The following DNA sequence Seq-2405 <SEQ ID NO. 70> was identified in *H. sapiens*:

TCCTGAAGTCAGATAGTAGGAGTCTTCTAAATTTGTTCTCTTTCAGAAGTATTTTGGCTT

TTTTATTCTTATGAATTTTCGTGTGAATTTAGAAACAGCTTGTGGATTTTAAAAGGAAAT
GTCTGCTTGGATTTGAATGGAATTGCGTTGCATCCAGATCACTTTGAGGAAATTTGTATC
TTAATTCTATTGAATTTTCCAACAATAGACATGATGTAGCTCTCTGTTCAGCTCTTCTTT
GATTTTTTAAATAGACATTTACAGTTTTTGGCACAGAATCTGTATATGTTTTGTTAGATT
TATAGCTAAGCATTTTATGTTTTTGATGCTGTTTTAAAATTTTAATTTCCAACTGGTCAT
TGCTGCCATACAGAAATAAAACAGAAATACAGAAATACAGGGTACAAAATAAACTTGACC
TTGTTTCTTTCACTCTAGATAGTATTGCTTATTAGTTCTACTAAGTTTTTGGTAAGTTCT
TTGAGATTTTTCTCCACAAGCAATCATGCTAACTAAAAATAAAAACAATTTTGTTTT

The following amino acid sequence <SEQ ID NO. 204> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 70:

NKIVFIFSHDCLWRKISKNLPKTNAILSRVKETRSSLFCTLYFCISVLFLYGSNDQLEIKILKQHQKHKML
SYKSNKTYTDSVPKTVNVYLKNQRRAEQRATSCLLLENSIELRYKFPQSDLDATQFHSNPSRHFLLKSTSC
FIHTKIHKNKKAKILLKENKFRRLLLSDFR

The following DNA sequence Seq-2406 <SEQ ID NO. 71> was identified in *H. sapiens*:

AAAAATAAAAGTTATGGATCACAGCAGATCATAATAGAGAATAGTCCATCTCTCCTAGAA
AATTTTTAAAAATAAATCTTAGAAACTGCATGGGAAATACTGTAAAAACAAAGGTTATTG
TCCTCAGCTATGAATTAGAATAAATTTGGCACTAGATTATGGGGTATTCCCACAGGAAAG
TACCTTACTGATTTTCCCTCTATCCTTCTTGATACATTATGGTTGAACCCACTGTTATGC
AACACCTGCTTACTTTGGCCTTAAGGGTCATAGTGACAAAAGAGAAACCTTTAAAGAAGT
CATAGTAAATGTTAGGGAAAGGGATTTTCAATGCATGGATATATTTGGCAAGGTAAACAA
AAAGTTGCCTGATAGCAAGGGAGGAGGCAGGCCACTGTGAATAGCAACTTATACTAGTCA
ATATTGAAAAGTAAAAGCAGTTGAATGGTTTCAAAGTATATAAGAATACAAACTGATTGC
TTATAAAATGTTTTTTAAGTAGAGACTGCACTTTAATGTGAGATGAGGCGGATCTATACA
TTAATTTTATATACGCAAATGATCCTACTTACATTCTTGAAAATAATTTGACTCTTTAGG
TGAACCAACTGAAATCTCATTTACACTGTTGATTTGCCTAGTAAATAATTCTCTTTAGTA
TGAGAAAATCAAAGAAGTTTGAAGTGGAACAAATTCTAAATTACTAGAATATGATTTAAA
TGGCTAGGAGAATATTATAAGGGGTATAAAACAGAATATTAATCCAAATATTTAAGATGC
TAATTCTGGGTAAAAGCTATTTTTGAGATGACATGAATTTTCAAAATACTAAAATTTTTA
AAATAATCATTTCCACAAACTTATTTAAGCTGTGTGTAATGTATGTAAATACTAAGTAAT
ATGTTATTCAATTTTAGGAACTTTATGTATGTTTTCATACTAGTATTAGAAAATAATTCT
GAAAGGAAGATGAAAATGAAAATATTCATTTAGGTTAAAC

The following amino acid sequence <SEQ ID NO. 205> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 71:

VPKIFSFSSSFQNYFLILVKHTSSNITYYLVFTYITHSLNKFVEMIILKILVFKFMSSQKLLPRISILNIW
INILFYTPYNILLAIIIFFRICSTSNFFDFLILKRIIYANQQCKDFSWFTRVKLFSRMVGSFAYIKLMYRS
ASSHIKVQSLLKKHFISNQFVFLYTLKPFNCFYFSILTSISCYSQWPASSLAIRQLFVYLAKYIHALKIPF
PNIYYDFFKGFSFVTMTLKAKVSRCCITVGSTIMYQEGRENQGTFLWEYPIICQIYSNSLRTITFVFTVFP
MQFLRFIFKNFLGEMDYSLLSAVIHNFYF

The following DNA sequence Seq-2407 <SEQ ID NO. 72> was identified in *H. sapiens*:

ATGATATTCCTATTGGATGGTGCTAATCTGGTGCAGGGTTTCTTAACCTCAGGACTACTG
GCATTTTGGGTCAGGTCATTCTTTATTGTGTAGGGCTGTTCTGTGGATTGTAGAATGGTA
AGCAGCCTCCCTGGCCTCTATCCACTGGATGCCAGTTATACCCGCTCCAGTTGTGACCAT
CAGAAATATCTCCAGATAAAATACCAAATGTCCCTTGGGGGAGAAATCGCCCCCAGTTGG

GAACCGCTAGTCTGGAGAAACTCCAAGATTTAAAGGTTGTAGAAGAGAAAGAGCTGCCAG
AGAAGACTGAAAGGGCAGTGGAGGAGAGTGGGGTGTGTGTGGGGGGGTGTGGGCAGGAGC
CAAAAGAGTGTTTCAAGGACTTGGTCATGATCCTTTTAAAATGCCAGTCAGATCATGTCA
CTTCCTGCTCAAAACCATCCACACGCTTCACATCCCATTTGAAATAAAATGCCAACTGCT
TACCATGCCCTATACACAGAACAACTGTAATAACCTGGGCACCTTTGAGAGTGAAAGGAG
GCAATACTAATAATCATGCCAGGGCAGTTCAGGGCACACTGGAGGTACCATCTCCTAAGC
TCAGGCCCCTGCCCATCTCTCCAGCTTCATCCCCAACCACTTTCTGCCTTGTCCACTCAC
CCACGACAGCCTTCTTGCCATTTGTATTGGGCCATTCTCACATTGCAGGGGCCAGAGCTT
AGGATGACAAACATATAGCAACACATATAATGTAATGTCAGTGATATTAATAGATGCTGT
GAAATAAGATAAAGTGAGGTGGAGACATAGGGTGACTGGGGGATTGGTGGCTATTTTACT
TAGGGGTCAGGAGATCGTCTCTGAGGATGAATCACTTATGCAGAGACCCGAATGGAGAGA
GGGAATCTAAGAAGATCTGGGGAAGAGGATTCCAGGCAGAAGGAACAGCAAGTGGAAAGC
CCTGAGGTAGGAACAAGCATGGAATATCAATAGAATGGTG

The following amino acid sequence <SEQ ID NO. 206> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 72:

PFYYSMLVPTSGLSTCCSFCLESSSPDLLRFPLSIRVSAVIHPQRRSPDPVKPPIPQSPYVSTSLYLISQH
LLISLTLHYMCCYMFVILSSGPCNVRMAQYKWQEGCRGVDKAESGWGSWRDGQGPELRRWYLQCALNCPGM
IISIASFHSQRCPGYYSCSVYRAWAVGILFQMGCEACGWFAGSDMILAFKDHDQVLETLFWLLPTPPHTHP
TLLHCPFSLLWQLFLFYNLILEFLQTSGSQLGAISPPRDIWYFIWRYFWSQLERVLASSGRPGRLLTILQS
TEQPYTIKNDLTQNASSPEVKKPCTRLAPSNRNI

The following DNA sequence Seq-2408 <SEQ ID NO. 73> was identified in *H. sapiens*:

TTCCTATTGGATGGTGCTAATCTGGTGCAGGGTTTCTTAACCTCAGGACTACTGGCATTT
TGGGTCAGGTCATTCTTTATTGTGTAGGGCTGTTCTGTGGATTGTAGAATGGTAAGCAGC
CTCCCTGGCCTCTATCCACTGGATGCCAGTTATACCCGCTCCAGTTGTGACCATCAGAAA
TATCTCCAGATAAAATACCAAATGTCCCTTGGGGGAGAAATCGCCCCCAGTTGGGAACCG
CTAGTCTGGAGAAACTCCAAGATTTAAAGGTTGTAGAAGAGAAAGAGCTGCCAGAGAAGA
CTGAAAGGGCAGTGGAGGAGAGTGGGGTGTGTGTGGGGGGGTGTGGGCAGGAGCCAAAAG
AGTGTTTCAAGGACTTGGTCATGATCCTTTTAAAATGCCAGTCAGATCATGTCACTTCCT
GCTCAAAACCATCCACACGCTTCACATCCCATTTGAAATAAAATGCCAACTGCTTACCAT
GCCCTATACACAGAACAACTGTAATAACCTGGGCACCTTTGAGAGTGAAAGGAGGCAATA
CTAATAATCATGCCAGGGCAGTTCAGGGCACACTGGAGGTACCATCTCCTAAGCTCAGGC
CCCTGCCCATCTCTCCAGCTTCATCCCCAACCACTTTCTGCCTTGTCCACTCACCCACGA
CAGCCTTCTTGCCATTTGTATTGGGCCATTCTCACATTGCAGGGGCCAGAGCTTAGGATG
ACAAACATATAGCAACACATATAATGTAATGTCAGTGATATTAATAGATGCTGTGAAATA
AGATAAAGTGAGGTGGAGACATAGGGTGACTGGGGGATTGGTGGCTATTTTACTTAGGGG
TCAGGAGATCGTCTCTGAGGATGAATCACTTATGCAGAGACCCGAATGGAGAGAGGGAAT
CTAAGAAGATCTGGGGAAGAGGATTCCAGGCAGAAGGAACAGCAAGTGGAAAGCCCTGAG
GTAGGAACAAGCATGGAATATCAATAGAATGGTGATATGG

The following amino acid sequence <SEQ ID NO. 207> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 73:

ISPFYYSMLVPTSGLSTCCSFCLESSSPDLLRFPLSIRVSAVIHPQRRSPDPVKPPIPQSPYVSTSLYLIS
QHLLISLTLHYMCCYMFVILSSGPCNVRMAQYKWQEGCRGVDKAESGWGSWRDGQGPELRRWYLQCALNCP
GMIISIASFHSQRCPGYYSCSVYRAWAVGILFQMGCEACGWFAGSDMILAFKDHDQVLETLFWLLPTPPHT
HPTLLHCPFSLLWQLFLFYNLILEFLQTSGSQLGAISPPRDIWYFIWRYFWSQLERVLASSGRPGRLLTIL
QSTEQPYTIKNDLTQNASSPEVKKPCTRLAPSNR

The following DNA sequence Seq-2409 <SEQ ID NO. 74> was identified in *H. sapiens*:

AAGCTTACCCTGGCTGCTTACACTCTTATCCAATGCCATTTACCTTGTGTGATACATAAT
ATCTTGTATGAATCCTATTTTCTCTGTGTTTGTGTACCTTTCTTTGAAGAATATGACCTG
TCTCAATAATTCTTTTAATGTTTTTCTCTTAGTCCTTTTAACATCAGCAGGGCATTTGTA
GTGGTGACAGGAGAAACATAAACATATACCTCTTTTCTATTGCTTTTCTGCTATTTACAA
TAATTCTGTATGACTCTGAAACAAAAGAACAATTACCTGACAATTTCTTTCTGAGTCCTA
TATTCTGGCTTTCATATCCAATCTCCTTTTATCATGCTATTACCTCTCTTTTCTTCTGTC
TTTGAGGATGGGAAAATTCATCAACACCCTAAATACCAGCCAGAGAGGAAAAAAGAGTCT
GGATGGAGGCAGGACTCCTTTCAAAGCTGAATCTCAAGCACTGATCACGGAGCAGCAGCA
AAGAGACACTCAAAAAGAGTGGAGAGAGGAAAAACTAGCTGATCTCTAAGGTGTCTTCCA
TTCAAATTCACTATAATTATAAGAATGTGATTACTGGAGGAAGAACAAGGGCAGGGGCAT
TTCTGCAACATGACGCAAAAAAATATTGACCTTAAATTTGATACATATGAACTTTCTAAA
TGTAGAGAGAAGCTACCTCCTTGCTGCACTTGTATGTGTGCCATTCATTTCATTTTAATA
AAAGTTTGTAAACATGAATGAATGCAGGGGACAGACCACCTCTTTATGAGAATGCAGCAT
AGTTCAGAGAAAGTCTATTTACCAAAAACTGAATACATGTTTATACTGAAATTTTAATTT
TTTCTATTTTTATTTTTAATTGTGATAAAATATAAATAACATAAATTTACCATCTTAATC
ATTTTTAAGTATACAGTTCAATAGTATTAAGTCCATTCGCATTATTGTGCAACCAATTTC
CAGAACTCTTTTTATCTTGCAAAAATGAAACTCTATACCC

The following amino acid sequence <SEQ ID NO. 208> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 74:

KLTLAAYTLIQCHLPCVIHNILYESYFLCVCVPFFEEYDLSQFFCFSLSPFNISRAFVVVTGETTYTSFLL
LFCYLQFCMTLKQKNNYLTISFVLYSGFHIQSPFIMLLPLFSSVFEDGKIHQHPKYQPERKKESGWRQDSF
QSISSTDHGAAAKRHSKRVERGKTSSLRCLPFKFTIIIRMLLEEEQGQGHFCNMTQKNIDLKFDTYELSKC
REKLPPCCTCMCAIHFILIKVCKHEMQGTDHLFMRMQHSSEKVYLPKTEYMFILKFFFLFLFLIVIKYKHK
FTILIIFKYTVQYVHSHYCATNFQNSFYLAKMKLYT

The following DNA sequence Seq-2410 <SEQ ID NO. 75> was identified in *H. sapiens*:

ACCACAAAGGCTAGAGGCATGGATTATTGGAAACTCTCTTCTGAAAAATTTTTTACTAAT
TTGGGAGATTAACAGTCAGAATCAATGGGTGATGGTTTATAGAGTGATACCAACCTTGTC
CAGTCCTGCTCATCATTTCCAATCAACAAAATGAATAAAGATGAAGAGAGTATGCTTATG
ACATCAGTGAATAGTACAGATCTCAGACTGCTGAAGAATGTACAAGATGACTTAGCCTGG
ATCCAAAAAGCCAAGCTGGAGAGGTAGGGTGGTTCCAACAAGACAAAATGTAAAAACGAA
GACCAATACTTAAGACCAAAAAGTCAAGCCAAACAAAACATGCTGATGTGGCTAAACAGC
AAGTTGTGCTAAAAAATAAGACTCAAGAAGTCAAAGGTCAGTTTTATATGAATCCAAAAA
GCCAATGCAATTTTAATTTGCTTTAATAAATATGTATTATCTGGAAAAAAACACATACTA
CAGTGAGTTTTCTGTGGAATGAAATACTAAAGCATGTTTTCTTGGAGAAAGAGTTTCCAT
GACCAAATAAGTTGGGGGATACTCCAAGTTGATATAAACAGGTTTATTTTCTACAGGAAT
ACTCAAAGTCGATATGGTGACTATTGCTTCTCAAAGTTATTTGAACATGGAACACTTCTT
TTTGTAGTACCTCTTGAGGCTGGTGTTAAAGAGAACACTCTTGAGAAAACACTGAACAAG
GGCTGTCTCAGGAGGCAGTTCTCTGTAAGTGGGACTCTTTTTAAAAACAGAAGAGATCCA
AACATCAGATGAGTGTTGGTCTAAATGACCATAAGGTTTCCTCCTACCCTCGAAGTCTGT
AATACTTGGTTATCCAGACCTAACAAACAATCCTAATTCCCCATGACACCTGGACCAGAG
TTTCTGATGAGAGAAACTCTAGAGAAATACTAGTAGCAGAGTAATGATTTAAAAAAAAAA
AAAACTTTTCCTCCAATGAGTGCATGCTTCAAAAGGGCTG

The following amino acid sequence <SEQ ID NO. 209> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 75:

QPFSMHSLEEKFFFFLNHYSATSISLEFLSSETLVQVSWGIRIVCVWITKYYRLRGEETLWSFRPTLICLD
LFCFKESHLQRTASDSPCSVFSQECSLHQPQEVLQKEVFHVQITLRSNSHHIDFEYSCRKTCLYQLGVSPN
LFGHGNSFSKKTCFSISFHRKLTVVCVFFQIIHIYSKLKLHWLFGFINPLTSVLFFSTTCCLATSACFVWL
DFLVLSIGLRFYILSCWNHPTSPAWLFGSRLSHLVHSSAVDLYYSLMSAYSLHLYSFCLEMMSRTGQGWYH
SINHHPLILTVNLPNKIFQKRVSNNPCLPLW

The following DNA sequence Seq-2411 <SEQ ID NO. 76> was identified in *H. sapiens*:

CTCCAGGATGCGCCCCTTCCCGGCACAGCCCACTGCCATATCTTGCTGGAACCTGGGTCA
TCGTCCATCGTCTATCACAGGCTCCGCCAGCCTTCGTGGATGCCATCTATGTCCGTGGGT
CTCACCCGTCTCGCCACCAGCTTCCACTACGACGCTGGACAGTACACAGGGAGCAGACGG
GGATTCCAGGAGGAAGCCACTGCAAATAGGGCCTGCAGCTGCCCTCTCTCCTTCTGAAAT
CCTAGCATAGTCCAGGACACAGCACCTCCCTGGCTGAGCAGCTGAACTGCCAAGCTCAAC
TCCCTGATTGAGCAGATATTCTGCAGAAATAGAAAAGGATGGAGGGAAGGCTTCTTCCCA
CACAATGAACATCAAACCCACCCAAGGGGCAGTGGCTGGGGCCTCCCTTCCCAAACAGCT
GGCTCAAAACATGCACAAAATTTTCCCAAAGTGGGCTGGGAGCAGGGCAGCTGGCTTCCA
CTTTCATATTACTGATGCATCCAGACATACTTCCATAGTGTTTAAAAATTTTTGGATGTA
TGTCAAATGCTCTTAAGAGTGCGATCTTAGGCATGTGGTAAATAAATATGATGTAATCCT
CCCGTCTCCAAGGGTGCTGCTGCCCTCTCCCTCCCTCCCTCACTGGTCCTGGGCAAGCCC
TTGACCTCCACGATCTCTCTGCGCCTCTCGTGACGCCCACAACAAGGGGCTGTGCCAAAG
GGAAAGGTAGAAAGAAAAGAGGATGTGCTGTGTGCTGTCATCATCCCTGTGCCAGAGACA
GGGCACAGGGTGGTGGCCTTGCACCACCGGCGCATCCCCCACATGGGGAAGCTGGGGTCA
CCCTGCACCACAGGCATCCCATCAGCCTCTGTGACACTGACAATGATTCTCGTGAATGGA
CAGGCTGAATGGTCCTCAGCCCTCTCTTTCTATGCTGGCTGAACTCTGAGGCGGGAACAG
GACAGACAGTGGCTGGAGGCCCTGGCAGGGAGGGCACCCT

The following amino acid sequence <SEQ ID NO. 210> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 76:

RVPSLPGPPATVCPVPASEFSQHRKRGLRTIQPVHSRESLSVSQRLMGCLWCRVTPASPCGGCAGGARPPP
CALSLAQGQHTAHPLFFLPFPLAQPLVVGVTRGAERSWRSRACPGPVREGGRGQQHPWRREDYIIFIYHMP
KIALLRAFDIHPKIFKHYGSMSGCISNMKVEASCPAPSPLWENFVHVLSQLFGKGGPSHCPLGGFDVHCVG
RSLPSILFYFCRISAQSGSAWQFSCSAREVLCPGLCDFRRREGSCRPYLQWLPPGIPVCSLCTVQRRSGSW
WRDGDPRTMASTKAGGACDRRWTMTQVPARYGSGLCREGAHPG

The following DNA sequence Seq-2412 <SEQ ID NO. 77> was identified in *H. sapiens*:

CTGTCAGTTTGGTGCCCTCGGCTACGCAGGGCCTGTTAGAAGGGTGCCCTCCCTGCCAGG
GCCTCCAGCCACTGTCTGTCCTGTTCCCGCCTCAGAGTTCAGCCAGCATAGAAAGAGAGG
GCTGAGGACCATTCAGCCTGTCCATTCACGAGAATCATTGTCAGTGTCACAGAGGCTGAT
GGGATGCCTGTGGTGCAGGGTGACCCCAGCTTCCCCATGTGGGGGATGCGCCGGTGGTGC
AAGGCCACCACCCTGTGCCCTGTCTCTGGCACAGGGATGATGACAGCACACAGCACATCC
TCTTTTCTTTCTACCTTTCCCTTTGGCACAGCCCCTTGTTGTGGGCGTCACGAGAGGCGC
AGAGAGATCGTGGAGGTCAAGGGCTTGCCCAGGACCAGTGAGGGAGGGAGGGAGAGGGCA
GCAGCACCCTTGGAGACGGGAGGATTACATCATATTTATTTACCACATGCCTAAGATCGC
ACTCTTAAGAGCATTTGACATACATCCAAAAATTTTTAAACACTATGGAAGTATGTCTGG
ATGCATCAGTAATATGAAAGTGGAAGCCAGCTGCCCTGCTCCCAGCCCACTTTGGGAAAA
TTTTGTGCATGTTTTGAGCCAGCTGTTTGGGAAGGGAGGCCCCAGCCACTGCCCCTTGGG
TGGGTTTGATGTTCATTGTGTGGGAAGAAGCCTTCCCTCCATCCTTTTCTATTTCTGCAG
AATATCTGCTCAATCAGGGAGTTGAGCTTGGCAGTTCAGCTGCTCAGCCAGGGAGGTGCT

GTGTCCTGGACTATGCTAGGATTTCAGAAGGAGAGAGGGCAGCTGCAGGCCCTATTTGCA
GTGGCTTCCTCCTGGAATCCCCGTCTGCTCCCTGTGTACTGTCCAGCGTCGTAGTGGAAG
CTGGTGGCGAGACGGGTGAGACCCACGGACATAGATGGCATCCACGAAGGCTGGCGGAGC
CTGTGATAGACGATGGACGATGACCCAGGTTCCAGCAAGA

The following amino acid sequence <SEQ ID NO. 211> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 77:

CQFGALGYAGPVRRVPSLPGPPATVCPVPASEFSQHRKRGLRTIQPVHSRESLSVSQRLMGCLWCRVTPAS
PCGGCAGGARPPPCALSLAQGQHTAHPLFFLPFPLAQPLVVGVTRGAERSWRSRACPGPVREGGRGQQHPW
RREDYIIFIYHMPKIALLRAFDIHPKIFKHYGSMSGCISNMKVEASCPAPSPLWENFVHVLSQLFGKKGGPS
HCPLGGFDVHCVGRSLPSILFYFCRISAQSGSAWQFSCSAREVLCPGLCDFRRREGSCRPYLQWLPPGIPV
CSLCTVQRRSGSWWRDGDPRTMASTKAGGACDRRWTMTQVPAR

The following DNA sequence Seq-2413 SEQ ID NO. 78> was identified in *H. sapiens*:

TATATTTTCTGGATTTACATGCCAGGTTACAAAAGGAGACCCACACGAAATCCCTGAACT
CCTGTGCCCACCCAGAGATTAACATGGAGAGGTCAGGGGCTGTTTTCTCTCCATAGGCTT
CAGTGGCCTGGATGTCTGAGTTTTCAGAGACAGGATAAGTCCACATATTATTTTTAAACA
AATTTCTTACAACTCAAAAGCTTTCATATCTTACTTTCTTGGTAAGAGTCAAGTTTATTA
TCCACGTCCATACAAACACAGCTGGCTACACAAACTGATCTAGGACAAAAAGTCAGAAAC
ATGGGGCCATAGGATTCTGGGTAAATGTGCTTTCTAACAAAAACTATCATATTTACAGAA
AAGCAGACAAAGTGATGAGAGTCTTCTGCCTTTAGAATTAGCTGACTTTAAAAATTAATT
TAACTCTGACATGTGACAAGAATTTTATACATCATTGCAAAATTAAAAAGGCACTTTGGA
GTGGAAGTACTGATTACAGCATATTTTTGATAGAGATAATGGACTTTATTTAAAACACAT
TCTACCATTTTCTCCTGTGTTTTTCTTTGAGTCCACAGAGGAAAGTTACTACACAAATTC
AGGTTATTTTTATTGACGGTTATGTTATGGTGAAGCTAGATGAATAGAGTTTAAAGTTAA
GTTTTGTTGGGTATTTCCAGGCCACTTGGCACATCAAACAGGTAAGCACTTTTTCTCAAA
GAAAAGTGTGTTGTATTGATCTTGCTTTGCTCTAGTATTGACAATTATATGAAATTTTAA
GCATCTCCTTAGAATTCCCAGCTTTTTGAGGGCCAATTTCTATTCAGGTTTTTATGGCTA
ATCTCTTATGACATCTGTCATTCCAAGTATTTAAACTCTCATATGTTTCTTTGGTGTGCA
TTTTTTCATTTGTTTAAGCTCGTTTCTTAGGTCAGTGAGGGTGTGTGTTCTTTCTTTTAT
ATCACAGGGCTTTGTCCACAGGGTAGACTCAGCTCATGTT

The following amino acid sequence <SEQ ID NO. 212> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 78:

HELSLPCGQSPVIKKEHTPSLTETSLNKKNAHQRNIEFKYLEQMSEISHKNLNRNWPSKSWEFGDANFILS
ILEQSKINTTHFSLRKSAYLFDVPSGLEIPNKTLTLFILHHNITVNKNNLNLCSNFPLWTQRKTQEKMVEC
VLNKVHYLYQKYAVISTSTPKCLFNFAMMYKILVTCQSINFSQLILKAEDSHHFVCFSVNMIVFVRKHIYP
ESYGPMFLTFCPRSVCVASCVCMDVDNKLDSYQESKIKLLSCKKFVKYVDLSCLKLRHPGHSLWRENSPPL
HVNLWVGTGVQGFRVGLLLPGMIQKI

The following DNA sequence Seq-2414 <SEQ ID NO. 79> was identified in *H. sapiens*:

GAAAGCTGACAAAATTACATTTCTTGAGTCCAGTATCTATTCTTTAATTGTCTTCCTTTA
TATTTGAACTCTTAGTCAACTGTGGTCCAAAGAGCATTCAACTGAGGAGGGAGGCTCGCT
AATTTTCCCTCACCTAGTGACGCCCATGCTTGAGCTTCATGAAATTTAAGATAATTATTA
TTATATAGTTATATAATCATTTCATGTACTATCTTTTTCTTCTTCTTTACTTTTATTTTT
TAAAAGCAGAAAACAATAAAATGGCCATCAATTGCATGAACACTGCTCTAAAAAGATAAC
AGTAAGACCGAACCTGAACTGTTGGCTACCTGGCCGTGCCATATTAATAGCTTACAAGGA
TCAGATATAGAAATATCAATCACAGGTTGTGTAGAGGTGTCCATGTACAGAGCACAACAT

TGTATATTAAAAGGATGTTGAGCTTTTATAATTATTGCTATGGTTTTATACAGTGTAATA
AGCCCATGATAAATAGGAGCTCATATTTTATCTTAATGAAGTGCTATTTTATATTACTTA
TTGATTTATGTTTTTCCCCCAAGAAAGTTTTAACCTTCTGAGACTTAGAGACTCATTTAA
ATGCTTTGACCCCCCATACCCTCTTTGCAGGGTGCAGGAGGATGTGTATGATCTTAACCTT
TACAGCAAATCTCTTCTTTTGGATGGGGTATTGCAATTTTCTTTTAGAGGATCACACTTA
GTCCAGTTCAATGTAGTTTAGAAGGGGCTGACTTCATCTCTGGTTCCATGGGTGGACGCT
TGATCCACTCTGGTTAAGCAAAATACTGCATCAGTGTAACTCATTTGTGAATGGGTACAT
GATCCAAGCTGGACCAATAAGAGCCCTACCTAGAGTTTTGCTTGAATTGTTAGGATAAAG
GGAAATTCTTTCCTGAAGCACCAAGGTTATTTTCTGGAGAAATCATGACCAAGAGTGAAG
CCAATGCATGGAAAACAAAAGCCGTGAGTAAAAAAAAAAG

The following amino acid sequence <SEQ ID NO. 213> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 79:

KADKITFLESSIYSLIVFLYITLSQLWSKEHSTEEGGSLIFPHLVTPMLELHEIDNYYYIVISFHVLSFSS
SLLLFFKSRKQNGHQLHEHCSKKITVRPNLNCWLPGRAILIAYKDQIKYQSQVVRCPCTEHNIVYKDVELL
LLLWFYTVAHDKELIFYLNEVLFYITYFMFFPQESFNLLRLRDSFKCFDPHTLFAGCRRMCMILTFTANLF
FWMGYCNFLLEDHTSSSMFRRGLHLWFHGWTLDPLWLSKILHQCNSFVNGYMIQAGPIRALPRVLLELLGR
EILSSTKVIFWRNHDQESQCMENKSREKKK

The following DNA sequence Seq-2415 <SEQ ID NO. 80> was identified in *H. sapiens*:

ATGCATCATGTCTTCATTTTGTGGCCTCTAATAGATTCTTGGGATGTAAAAGAACTCATT
TTATATACATATGCAAATTTAAAACCTTCTATAATAAGTCTGACATCACCTGTGTCCTCT
CTGTGTTTGTGTTATCAGCAAGTGAATTTCTCAGTACTCCCACATCACAAACCCCAATTA
CCACTCCATATGTTTCCCAAATTAGTAGCTAATAGCGTTTTCCCAGGCGAATGTATCTAG
AAATACCCAGGGATTCACTGCTATACCTAAGTCAGCAATGGTTCATCTTTCTCCTTGCTG
TGGAGGAGAACTTGACCAGAGGAGTCCACTTCCCCTGGCCCGGCAGCTTCTTGCATGGGA
AACTAGCTGCTCCTGCTGCTACTTGGCTGATGATTTACCCTATAGCACATTTTATCTTTA
CGTAAACACACAAAGTCCTTTCACGTCTTTGTTCCTGTTCCCATGCCATGACTCCTTCCT
GGAATACCATTCTTTTATTCTTACTCACTAAATAAGCTCTTCTACTCCTTTTCTTCGGGC
CCCCTTCCTCTGATTCAGCTGAGAAACAACTACTGTCTGTCTCCATCAAAGCTAATTTTC
TGCCTCCTGTTTTCCCACCATACTTTGCCATTCTAGACATCTGTTGCATATCATTTTTTC
TGTTACTTAACTAATGCATCAGTCTTCATTCATTCTCCTCCCAGACTATACTCCTCCTGG
GTTCAGAGCATATCTCATTCATTTCTGTGTTACCTTTGCTTATCTCAGTGCTGGCTTCAG
AGTAGATACTTCAGAGATGCTATTTAAATCAGAGTTAGGGTAGTTAGAATAGGAGAGAAT
GAGGACTCTATGGTGCTCAGGTGCCATGCATCCTGCAAAGAGAACATGAAAGGACATTTT
TTTTTCCTTCAATAATTACATGGACTCCTTCAGTGATCCCTGTGTCTGTTGGGCCTTGAG
TAATTACCTGCAATCTCTGTCTTTGTGAGGCTATTAATTA

The following amino acid sequence <SEQ ID NO. 214> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 80:

MHHVFILWPLIDSWDVKELILYTYANLKPSIISLTSPVSSLCLCYQQVNFSVLPHHKPQLPLHMFPKLVAN
SVFPGECIKYPGIHCYTVSNGSSFSLLWRRTPEESTSPGPAASCMGNLLLLLLGFTLHILSLRKHTKSFHV
FVPVPMPLLPGIPFFYSYSLNKLFYSFSSGPLPLIQLRNNYCLSPSKLIFCLLFSHHTLPFTSVAYHFFCY
LTNASVFIHSPPRLYSSWVQSISHSFLCYLCLSQCWLQSRYFRDAIIRVRVVRIGENEDSMVLRCHASCKE
NMKGHFFFLQLHGLLQSLCLLGLELPAISVFVRLLI

The following DNA sequence Seq-2416 <SEQ ID NO. 81> was identified in *H. sapiens*:

GCCAGTCAATGCCAAAGACATTCTGTTCGGTTTGGAATGAATAAAACTTCTGATGCCCAT
ATGGTAACCTTATGCTTTGAGAACTCTTCTATAGCACAATAAAATCTGAGCCGTCAGAGT
AACTAAGTGATGGAAAATGAATAACTAAATGTATAGGGAAAGAATCCAGAAAAGAAATTT
GTATTTTATTTTTTCTAAGTAACTTCCACAGATATGTTTGAGAAAACTGTATGATCTAGT
GAATAGAATACTCAAAACTCTAATATACAAGTCACAGGTATGGGCCCTAGTTACTTCACT
AAATGACTGGCTTTAGGCAGATAACTTGTCTGGTTCCAGTTACTAACTATGAGAAATAGA
AAATACATCATTACCTTTCTATAATAGTCCACAACTATTTCAGCACACCCAATGTGACAA
AAAACCGTCTCAAGCCCACTTCAGTAACAACTGAGAATTTGTGGGTTCATTTAAATGTCA
AGGCCAGCAGTAAGTGAGGGCTGGTTCTGAGGCTGACATATTCTGAGGAGAACATGGTCT
TGCTTTCTCTTTTCTGGGCACTTTTGTCCTCTGGATGGAATCCATTCTTGGGCAGGCTGA
AGTCCTTCTCTCATGGTGGCAAGATGGATATGCCAGGCAACCATCCTGTCTGCAGAGAGC
CTGCCTAGTGAGAAGTTTTGGGATTAGTTCTGACTTGATGAATTTGGGTCTCATGTTTAT
CCCTGGATATATCTCTTTTGCTCAGGTGAATGGATATGTTGACTGCCACACCTGGGTTTC
TGTGACTACTCCTGGATTCAGTGATGGAGTCAGCCCCAAGTAAGGCCCATAAACAAGGGT
GGAGGAGAGTGGTTCCTGGAAAGAAAGTCAGGGTAAAGGCAAGGGGACAAATGCCAGATG
GGCAGTAAATGGCAGCTGTCCAAATTTTATGCCTGAACCACTGAAAGGAATCTTCACTCT
CACTGTGGGTATTAACATAGGACGCGGTGATGCTTAATGG

The following amino acid sequence <SEQ ID NO. 215> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 81:

PVNAKDILFGLEIKLLMPIWPYALRTLLHNKIAVRVTKWKMNNMYRERIQKRNLYFIFSKLPQICLRKLYD
LVNRILKTLIYKSQVWALVTSLNDWLADNLSGSSYLEIENTSLPFYNSPQLFQHTQCDKKPSQAHFSNNEF
VGSFKCQGQQVRAGSEADIF<u>GEHGLAFSFLGTFVLWMESIL</u>GQAEVLLSWWQDGYARQPSCLQRACLVRS<u>F</u>
<u>GISSDLMNLGLMFIPGYIS</u>FAQVNGYVDCHTWVSVTTPGFSDGVSPKGPTRVEESGSWKESQGKGKGTNAR
WAVNGSCPNFMPEPLKGIFTLTVGINIGRGDAW

The following DNA sequence Seq-2417 <SEQ ID NO. 82> was identified in *H. sapiens*:

ACTAGCTTGGATGCACAAGGATTCAAGGATGCATAGTTAGCAAGTAGCAAAGTAGTTATC
AAGCCTAGGCGGGCGCTGACTCCAGAATTCAAGCCCAAGGTCACTTCTCTATACTATTTT
ACATTGTATTTAAGAACTACATGAACATGAATGCATGGTGTGATGCTTATAGTTTCCTGA
TGCTTATAGTGTCCTGATCCTACTTCTGCATAAGCCATGCAAAGGTAGTGACCCAGACTG
TAGAAATGCGTCAGAGTGAGATATACCAACAAAATGAAACGAGTGAAAGTAGTATAATTT
TCCAACATGTATACACTCTCTCACACACACATACACGTGAGAGGAGAACTAAAGATTAGT
GACAGGGGATTTATAACATTATAAAATCTGAGAGCCTGAAAACAAAGATCCAAGGCAGAG
CTAGAGGAACACAGGTATGGGTCAGTCAGGTGCAAGTTGAGAACACAGTGATAGGGTTCA
GAATGGTTAAGTATAAACAGAACTAGTGTGACAGAAGTCATTCTTACATAATATTTTTTT
AGTTGGTACCAAGATGGAGTAGATGCAGTATGTGGTAGTAAAATCACAGGTAATTAACTA
AATTGTTAAAAATTGAAATATTGTGCTCATTACTGATTTGTCTCCAATATTTATCTCTGA
TAGTCAATAAATCAAAATATATCAAAGCTTAAATTGTCAGAATAAAACCCATGTTTGTAT
AATTGCAGAAAAATTATTGAAAAGCAAAACTTGTCAGGGAATCCACGTGTTATCATTGCA
CAGCTCATATGAATCTGAAAAGTCACAAATAAATTAGCAACATGGAGTTAATTGGTTTTT
CTTTTTTTGCTTTACTGTTATTTTTCTTTACCACATGCAATTTCTTTTCTGGTTTTTGTT
TTATTATGGAAACAATACACTCTTTTTTCCTAATATTTATGCTTCTGCATCCTTGCTTAT
GAGTTTCTTCTTACATGAATGCTGTCGTCCTTCTTCCTCC

The following amino acid sequence <SEQ ID NO. 216> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 82:

RKKDDSIHVRRNSARMQKHKYEKRVYCFHNKTKTRKEIACGKEKQSKKRKTNLHVANLFVTFQIHMSCAMI
TRGFPDKFCFSIIFLQLYKHGFYSDNLSFDIFFIDYQRILETNQAQYFNFQFSLPVILLPHTASTPSWYQL

KKYYVRMTSVTLVLFILNHSEPYHCVLNLHLTDPYLCSSSSALDLCFQALRFYNVINPLSLIFSSPLTCMC
VESVYMLENYTTFTRFILLVYLTLTHFYSLGHYLCMAYAEVGSGHYKHQETISITPCIHVHVVLKYNVKYR
EVTLGLNSGVSARLGLITTLLLANYASLNPCASKL

The following DNA sequence Seq-2418 <SEQ ID NO. 83> was identified in *H. sapiens*:

CATGGCCCCAAATTAGTTTCCCACCTTATGTTCCACTAGTTTCATAGACAAACCTCTTCC
TGCCATACTGGTCTGGTCAGTGCCCTCCAGACACTGCAGTACTGCCTTGAACTGGTTTGC
TGTCATCTTTTCTCTCTGTCATCTAAATTCTAGCCTGTCTTTGATGGCTAAAAGCCTAAC
ATCTCTGTGGGCCTCAGAGAAATTATCTTCCTCTGCATTCCTCCAGTTGGCATCTCTCAC
TAATGGATTAATCATATTACCCTCTCCTATTGTTATGTGCTTTTATGCATATAATCTTAG
CCCCCCCATAGGACCAACTGTAATCCCTTTGAGGACAGGGGTTTGATCTTGTACCTATTT
ATAGTTCCCCACGTGCCTAGAGCCTCTTGCACACTGTAGGCTGGGGGAAAATATTTGCTT
ATGCTGATGATCTGAGAAAGATAATACTGCAAACAGGAGAAGTAAAGATTTCTTTGTCTT
GTTCCATTTGGAATGAATTAGTGGCAGGTAATCAGTTAGAGGTCAGTTCAGAAGGTTAAA
ATACGTGGACTTATCCCCTGTTACAGGTCTCTTATCTTTACAAAGATTGTGTTCCTGTTA
CTAACCTCTTTCTAAATCATTGGTGTTGTTATTTACAAGAAGGACTGGGCCAAATATGTG
AGGAAACATCAATGTATACTCATCCCTACCATTTGAAAAACAAGTTTTAAGTGTGTGTAC
CACTGATGAAGTATGAAGAATAACGTTCCCATTCATTCCAGAGTACTCAGGCCCTTTGCC
TGGGACTGCTAGCTACACATGCAAAGTGAATTCTATATCAGCATTTTGTAAAGCCCACTA
TTCTCACCGTACCAGCTTAACTGCAACCAGTTATTTAATAGGATTCTAATTAATTTAATT
CTCCACTGGTAGCAATTTCTGATGCACAATGTCTGTGCCTTTTACCTCTTTGCATCCCTT
CCCCAGCACTTAACTCAGCAGGTTGCATATAGCAGGAACC

The following amino acid sequence <SEQ ID NO. 217> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 83:

WPQISFPPYVPLVSTNLFLPYWSGQCPPDTAVLPTGLLSSFLSVIILACLWLKAHLCGPQRNYLPLHSSSW
HLSLMDSYYPLLLLCAFMHIILAPPDQLSLGQGFDLVPIYSSPRASLLHTVGWGKIFAYADDLRKIILQTG
EVKISLSCSIWNELVAGNQLEVSSEGNTWTYPLLQVSYLYKDCVPVTNLFLNHWCCYLQEGLGQICEETSM
YTHPYHLKNKFVCVPLMKYEERSHSFQSTQALCLGLLATHAKILYQHFVKPTILTVPALQPVIDSNFNSPL
VAISDAQCLCLLPLCIPSPALNSAGCIQE

The following DNA sequence Seq-2419 <SEQ ID NO. 84> was identified in *H. sapiens*:

TAACTTGTTCCAGCACAGATTCAAAAGTCTAAATTCTGAAGTCTCAACTAAATGTCATCT
AAACCAGATGTAGGTGAGACTCAAGGTATGTTTATTCTGAGAGAAATTGCTCTCCATCTG
TGATTCTGTGAATCAAATAGGTAAAGAGCTTCCAAAATGCAATGGTGGGACAGACATAGA
ATCGACATTCCCATTCCAAAAGGGAGAAGTAGGAAGGAATACTACAACAACAACAAAGTA
AACGATAAATCTTAAGGCTCCAGAATAATCTCCTTTTGATGCCCCATCTTCCAATCTTCC
AGGCACACTTGGGCAGGCGTTGGGCCCCCAAGGCTCTGGGTGTCCCAGTCCCAGCCCACA
TGACAGCACTTACATATTAGAGCCACATGCCAGGCTGGAAATGCCCTCTAGTGGCTCTAC
TGGTCTATGGTCAGAGGGTAGGCCTGCTCCTATGACTCTGCCAAGCACAGCCTTAGTGGA
GGCTTTTTGTGGTGGCCCCACCCCTATGTCAATTCTTTGCCTGAGCCTCAAGACTTTCCA
GGGCATCCTTTGAAATCTGTGTGGAGTCAGCTTTCCCTCTATGGTATTGCACTGTGTGTC
CTGGTGGAGATGATACCTAGAGAACATTACCAACGTTTATCATCTGTGCCCTCCAGAAAG
GTGGCCACTGGAGCCCACACCACACTTGGACCCTCTGGAGCCATGCCTGGAATGACTGAG
CAGTGCTGTGTCAGAAAGCAGGGAGCAGAGATGAGGTAGCATAGGGCAGGAAGTGCTGAG
CTCCAGTGGGCATCCTGGGCCCCTCTTTTGACCTTGTTCTGTCCCCTAGGCCTTGGCACG
CTGGGCCTGTGATGGGAGCAGCAGCCGTCATGATGTCTGAAATGCTTTTAGTGGGGGTCA
TTCCTCCATTGCCTTGATGAAAAGCACCTGGCTTCTGCAGTTCCATGTTAATCTGATCAA

ATGGTTGCTGGGCCACATCCTTGGTATTCTCTCCCAAACA

The following amino acid sequence <SEQ ID NO. 218> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 84:

TCSSTDSKVILKSQLNVITRCRDSRYVYSERNCSPSVILIKVKSFQNAMVGQTNRHSHSKREKEGILQQQQ
SKRILRLQNNLLLMPHLPIFQAHLGRRWAPKALGVPVPAHMTALTYSHMPGWKCPLVALLVYGQRVGLLLL
CQAQPWRLFVVAPPLCQFFAASRLSRASFEICVESAFPLWYCTVCPGGDDTRTLPTFIICALQKGGHWSPH
HTWTLWSHAWNDAVLCQKAGSRDEVAGRKCAPVGILGPSFDLVLSPRPWHAGPVMGAAAVMMSEMLLVGVI
PPLPKAPGFCSSMLISNGCWATSLVFSPK

The following DNA sequence Seq-2420 <SEQ ID NO. 85> was identified in *H. sapiens*:

CCACAGAAACATTCTTCAGTAGAACTTTAATATTACTGTCTTATAAAATTCTGTCAAATG
AACAAAAGATAACCCATAATTACACCCTAATATGACTGCTTTTAACATTTTACTGTATTT
CAGCCTTTTTGCTATGTATATAATTTTACAGAGTTGTAATCATACCCAGTATATGATTTT
ATCATGTTTTCCCACTTACCATTATAGGTATTTTTAATATTGCTACATAGTCTTCATGGT
TGTCATTGTTAATAGCTATGCTGTAATAGTTCACTGAATTGAAGTGCTTTATTTACTTAG
CTACCCTATTATCTTTAAACAATTTCTAATTTCTTTTTATAATAAACATGGACATATTTC
TGACAGGGGTGTTCTTTTTCACATCTTGACCTACTTTTCACATAGTGTTACAATTACCTG
ACCAAAGAATACAAACTTTTTGTCTCTTGACGTATATTTCCAAAAGATTTTTAAAAGGTG
CATTAATTTACTCTGCAGCTGGTGTAAATGAAGACCATTTTGTCATTGTTTTCTTGAGAG
TAGAGCTTCCAAAAGTAGGGATATGTGGCTAGGAGGAAGAAATCCAGCCTGGGGCAGGCA
TTCTGTAAAGAACTCCAGTTCTCACTGGTACACTGGTTTTATTTTTCTCTGTTTCTTGCA
GACTGAGCAATTGATAACTCTGTGGGTCCTCTTTGTTTTTACCATTGTTGGAAACTCCGT
TGTGCTTTTTTCCACATGGAGGAGAAAGAAGAAGTCAAGAATGACCTTCTTTGTGACTCA
GCTGGCCATCACAGGTAAGTAACTATGCAAGTGAGAGGCAGGAAGCTATATGTGAAGTCC
CTATGGCTTCCTGCTTTTAATGAATTTTATCAAAAAAAAAAAAAATGTAACGCATCGGTCA
ATTTGGGAATAATTTCTGAAAGAATATAAAACCTATATTTGAATATTTCCTCTGGCATAC
TTAACACATATGAATGCCTCTAAGATTTCATTATAAAAGT

The following amino acid sequence <SEQ ID NO. 219> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 85:

HRNILQNFNITVLNSVKTKDNPLHPNMTAFNILLYFSLFAMYIILQSCNHTQYMILSCFPTYHYRYFYCYI
VFMVVIVNSYAVIVHIEVLYLLSYPIIFKQFLISFYNKHGHISDRGVLFHILTYFSHSVTITPKNTNFLSL
DVYFQKIFKRCINLLCSWCKRPFCHCFLESRASKSRDMWLGGRNPAWGRHSVKNSSSHWYTGFIFLCFLQT
EQLITLWVLFVFTIVGNSVVLFSTWRRKKKSRMTFFVTQLAITGKLCKEAGSYMSPYGFLLLMNFIKKKKM
RIGQFGNNFKNIKPIFEYFLWHTHIMPLRFHYKS

The following DNA sequence Seq-2421 <SEQ ID NO. 86> was identified in *H. sapiens*:

AATAAGCAAATCTATTTTGACAGAAAGATTCATGATTGCTCCTGGCAGCAGGGGGTGAGG
AAGTTGGTGGGAAATGGGTACAGAGATTCTTTTGGCGATGATGAAGACGTTGTAACAGCT
TTTGAATTTTACAATCCAGAATTCTATTCTCTGCTAATTAGTCAAATAAAGGGCAGAAAA
TATACATTTTAAAACACAAAGATGCAGACATTACATTCCACATACAAGAGGATGTACCCC
AGCAAAACAAGGTGATAAACCAAGAAAGAGAAAGAATGGGATCCAGGAACAACAGCTTCA
ACCCAGGATAACAACAAAGGGAACTACTCCAGTGTTAACAGCTGGGCAGCCAGAGAGACA
GCATGTAGTCCTCATTGAAGCAGAAAGACAGAGGGTTCTGAGACAGAGGTCTCCAGGAAA
AAAAAAAAGAACCTGACTTACTGGATAAACAAGTCTTTAGTTTAAAAAACAACAAAAAAC

TGTATACACATATATATATAAAATCAGGTAGTATAAAGAAAAACAGAACTCCAGAGATTC
CTGGGTCACAGAAGGGGAAAGGGCTGTTCAAGAAAGTGAAATTGAACTAACTGAAAATAC
AGCTATCTTTATATTGGAAGGACAGTCAGGAAGTCAACAGATAAGGCCTAAACTGCATAA
AGCAGGAAACAGCAGACTAAAGACATTATTAAGAAATATGGAACACAACCAAAAGAAATA
GCAAAAACAATGAAAAGTGACTGTTTTTCATAAGTGAGGCAGGGGAAGAGAAGGGGTTAT
TTTTTTCCCCATTATATGTCTTTAAGAACTACTTGCTAAAAATATTGGGCACATATGAAT
TTGATAAAAGCGAAAAACTTTTTACTTCACAAGTGCAGCTTTAACATACGTTGATTACAG
TGAAGTTTTTGTTCTGTTAACCACTTTAGTAGGATTTGTCTAAATTTAGTGATTTACAAT
GCCTGCAGTAGAATCAGAAGATTTACACTGAAGGGATTAT

The following amino acid sequence <SEQ ID NO. 220> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 86:

IIPSVIFFYCRHCKSLNLDKSYSGQNKNFTVINVCSCTCEVKSFSLLSNSYVPNIFSKFLKTYNGEKNNPF
SSPASLMKNSHFSLFLLFLLVVFHISCLSAVSCFMQFRPYLLTSLSFQYKDSCIFSFNFTFLNSPFPFCD
PGISGVLFFFILPDFIYICVYSFLLFFKLKTCLSSKSGSFFFSWRPLSQNPLSFCFNEDYMLSLWLPSCHW
SSSLCCYPGLKLLFLDPILSLSWFITLFCWGTSSCMWNVMSASLCFKMYIFCPLFDLAENRILDCKIQKLL
QRLHHRQKNLCTHFPPTSSPPAARSNHESFCQNRFAY

The following DNA sequence Seq-2422 <SEQ ID NO. 87> was identified in *H. sapiens*:

CCTTCTCTTTCGGGTATTTTAGTCAGCCTCTTTTTATCGCTGTTATCACAGATATCCCCA
GAGACCACTTGTTATCATAATTTGCTAATGTTTCACAAAAGATGACCATTTAGTTTTTAA
TTAAATCTTATAGGACTTACACTCTCATTTGTTAGGCAAGGAAATTGAGCCAGGTCAAAT
TAAGTAAATTGCCCAAAATTCTCACTGTTTTTCCAAGTAATTTTAAAGAGTGACATCCAG
AAAATCTGTGACTTCTAGGAATACATTTAGAAAAACATATACCAGAGGGTTTAATTGCAG
CATTGTTTTTAACAGCAAAAATTGGAACTAAATACACATCAATTGGATACAGATAAATAA
AGTATGAGATATTCATGGACCAGAATCCTGTGCTGTAATTGAAGTGAATGAACTGGCAAT
GTGTGCACCAGTATCCCCAAATTATAATATTTACTAAAAAAAGCAAAATGCTGAATGATT
CATGCTGTATGATAACATTATATAAAGTCTGAGAACATGAAAAGCAACTGCAAACATAGA
TTATAGCTGCATAAATAAATAATAATAGTATAATAAACATTTGTAGGAATGGAATAGAGA
AAAACATTATGAGATCCAGAGTGCCCCAAAAAAACCTGCCCCCATATTTTAAATCAACCA
TTTTCTCATTTAACCCCATTTTTCCTCATCACTTACTATGTGACTAGATGTTCTTTGGTT
TTGTTAAAAAAACATTTCCGATTCCTTAACATACCTAAAAATATAATAAATTATTCTCTC
ATTATTTTCTTCTACATAATATACAAATTACTTCAAAATACGTACACAACTTACTTTCAC
ATAATATAATCTAACACAGTGGCTTTTCTTAGGTATGCATTCTACTAAAATCATATATTC
CTTTCTCTAATAATAAAAAGATTATATGACTTATAATTATATACTACCATAGCTGGGCTA
TCATAGTAGCCTTTCCTTTTAATATAAATACTTTGATACA

The following amino acid sequence <SEQ ID NO. 221> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 87:

CIKVFILKGKATMIAQLWYIIISHIIFLLLEKGIYDFSRMHTEKPLCIILCESKLCTYFEVICILCRRKEN
NLLYFVCGIGNVFLTKPKNISHSKGKMGLNEKMVDLKYGGRFFWGTLDLIMFFSIPFLQMFIILLLFIYAA
IIYVCSCFSCSQTLYNVIIQHESFSILLFLVNIIIWGYWCTHCQFIHFNYSTGFWSMNISYFIYLYPIDVY
LVPIFAVKNNAAIKPSGICFSKCIPRSHRFSGCHSLKLLGKTVRILGNLLNLTWLNFLAQMRVVLDLIKNM
VIFCETLANYDNKWSLGISVITAIKRGLKYPKEK

The following DNA sequence Seq-2423 SEQ ID NO. 88> was identified in *H. sapiens*:

GGGACATTTCATGCTGGGGAACATTTTAGGCAAATGGTCCCCAAGACCTTTTCGATAAGG

ATACTCCAGCGAAACAAATGAGACTGTTACAGGAGGCAGCACTGAGGCAGGGCAGGTGGC
ATTGGAGAACATGCACACCACCCCATGGGCACCGTGCAACACCACCCACCACCCATGGAA
GTGGTGACAACAGTGGGGAGGGGAAGCCTGTCAAGCAGATGTCACCAGGTGCTTCAAGCA
GTGTTGTAGGTCCCTGCTTATAGGTGCCAGGCCAACTCACCCACCTTCCTTCGACTCTTG
GAAAGAAAATAGTGGAGGTCTTTCTAAATCATGTGAGACAATAACTCCCCCAGAGGTGCC
ATCCTCTAGATTCCAGGGGATAAAGACGAGCACAAGAAGTACTGCTGAGCACTTTGTGTG
GGATGTGTGTCTAAACACGACAATCTGAAGACAGAGGTGTAGAAATTGGCAAGTTTCCTA
AAGCATGACAACACACACCCAAAACTCTTCCATAATGATTCCCTTTTTCCCTGTATTTTT
CCTGGATGCACCATCACTATGGGAACCAGGATGGTTACTCCCAATTCCCTGTCACCCACC
GCTTATTTAATAAACGATTTCTACTTTACTGAAATTGATGCTTCGTTTTCTTCTAATTCC
ATTCTATACTTTACCTCTGCTCTGAGTTACACTGAATTTATAACCCTTCTTTTAAACAGA
AGTCTTGCAAGAACAAACTACAGCAGTATCAGCAACCAACAATGCCACCAATACAGATTA
AAAAAACATTCTTATCTGAGGCCAGGTAACCAAATTTATGCAAAATAACTCAACAGATGC
TGGTCAGTACTAGCTGACCCATGAATTTAAGCTCTTACTTGGAAGAAATACAACCCAAAG
AGGAGAGAAAGGAAAAAAATGAGTCTCATATTAACATACAATAAAACCTTATTAACTGAT
AACTCCATAAATTATGAGTGGCAATCAGATAGATAATTCA

The following amino acid sequence <SEQ ID NO. 222> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 88:

NYLSDCHSFMELSVNKVLLYVNMRLIFFLSLLFGLYFFQVRAIHGSASTDQHLLSYFAIWLPGLRECFFNL
YWWHCWLLILLFVLARLLFKRRVINSVLRAEVKYRMELEENEASISVKKSFIKAVGDRELGVTILVPIVMV
HPGKIQGKRESLWKSFGCVLSCFRKLANFYTSVFRLSCLDTHPTQSAQQYFLCSSLSPGIRMAPLGELLSH
MIKDLHYFLSKSRRKVGELAWHLAGTYNTASTWHLLDRLPLPTVVTTSMGGGWCCTVPMGWCACSPMPPAL
PQCCLLQSHLFRWSILIEKVLGTICLKCSPANV

The following DNA sequence Seq-2424 <SEQ ID NO. 89> was identified in *H. sapiens*:

TATTATGTTATTGTGTAATTATTTGAATTATTGTCCCCTTTCCATCAATCCCCCAAACAC
ACACATATTAGGTGGAAATCCTTAGGGGCTGAGATGATGTTTTATTTACATCTGCATGCC
TGATGTTAAGCCCAGTGCTGGGCACGAATGCGATTTAGTGAGTGTTTCTTGAACATGAAT
AATGAATTCACCAGTGAAAGCATGAGTGGATCTGGTGGGGGCACAAAAGGCTGACTCCAG
GTTCCAGGAATCTGGGTGGAGAAACTTCTGGGCTGGAGGGAGCAGAGGACCACTGTGTTA
GGTCTACGTGGTTCTGGCTGGCAGGGTTAGCAAGGATGCAGAGGAGTTTCTGGGTCTTGC
TCAAATGATAATTTAAAACAACAATAATAATTAACATTCATTTAGTTCTTACTATGTGTC
AGTCCCTTATTGCCTTCTATGTATTCAGCCACTAATCCTCAAAATTCTAGGGGTTAGATA
TTTTTCCGGTCTATACTATACATATGAGAAAAAGGGTAGAACAGGGAGGTGCAGAAACTT
GCCCCAGGATACACAGCAAGTAAAATGGGAACTGGGATTGGTCACCTAGGGATTCTTGTT
TTTTAGATTTTGTTTTTTTAATCTCTCTATAGCCCCTTAGGTTATTTATTGATATTTTTA
CTTTTTATTTTGAAATAATTGTAGATTCACAGGAAGTTACAAGAGAGAGGTCCTGTGTAC
TCTTCACCCAGATTTCTCCAATGCTTAGATTTTATATAACTGTAATACAATATGAAAACC
AGGAAACTGATATTGGTTCAATATATGTGTATACTTCTATGCCATTTCATCATGTGTAGA
TGTAACCACCATCATGACCAAGCTGCAGAACTGTTCCATCACCACGAAGATCTGCCACCT
GTTGCTCCTTTAAAGTCATACCAGCCCTCTTCCCTGTCCCCACCCACTGTCACTATGCTT
AACCCTTGGTAACCACTAATCTGTTTTCCCATCTCTATAG

The following amino acid sequence <SEQ ID NO. 223> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 89:

LCYCVIIIIVPFPSIPQTHTYVEILRGDDVLFTSACLMLSPVLGTNAIVFLEHEIHQKHEWIWWGHKRLTP
GSRNLGGETSGLEGAEDHCVRSTWFWLAGLARMQRSFWVLLKFKTTIIINIHLVLTMCQSLIAFYVFSHSS
KFGLDIFPVYTIHMRKRVEQGGAETCPRIHSKNGNWDWSPRDSCFLDFVFLISLPLRLFIDIFTFYFEIIV

DSQEVTRERSCVLFTQISPMLRFYITVIQYENQETDIGSIYVYTSMPFHHVMPPSPSCRTVPSPRRSATCC
SFKVIPALFPVPTHCHYAPLVTTNLFSHLY

The following DNA sequence Seq-2425 <SEQ ID NO. 90> was identified in *H. sapiens*:

ATGCATACACCAGAGCCGACCCGCAGACTCTGCAACCCAGGCCCAGCTGCACGGTCAGTT
TGGAAGTCTACACAAGCATCTAGAGGACCTGGACACAAACAGGGCTAATTCAGGTGCCCA
ATTCATGTCCCAACTCTGTCCTGTCAGGCGACTAAGGCAGGGCTCTGGGAATCCAGGGAC
AGGTGGAGTAACTCGTACACAGTCAGTGTGGGAGTCTTAGCAGGTGACTGGGTCCTGCCC
GGACTCGTGTGGGATGGAGGGCTGGGTAAACTCATTGCTGCAATAAAAGGGACAGAATCT
CAGTGCAAAAGAGACTAGAAAAAATGTTAGGTTTCCAGAGAGAGGCTGGAATTCAGAGGG
GAAGATGGAAGCCCATTTGATATAGTAGTGGTGAAGATGGAAGGTGGCCCCTGCCGTGAG
GAAGACACCTGAGCTATGAAGAGTGGAGTATAAGCTTGGAACCAGATGTGCACATACCCA
GAGTTCATGTCCAACATATCTCAAAATCTTTGCAAAGTCTGTGTGGATCCTTAAAAACTG
GGGAGGGCAGAGCCAGCAGTGGGCAGGTGGCCCCCACCTGGAGGAATGGGATTATAGAGT
CCAGGAGTGAGGCAGCGCCCTACAGTTTGTCCTCATCCTTCCATTTTCCACACTTCCAGT
TTCCTTTCAACCACTTCAGAAAAAAAAAAAAGTCCAGAAAGTCTAATGTTGCCAAGTTTA
GAAACCAGGTCGTCATTAGTGTGAGTGGAATCAACGTTGATTACAGTCTGGTCCTTTTCA
AGTTTCTTTGATATCTTCAAAAGCCCAATCATCCTGTTCCATCTAGGACATTAAGAAAAA
TACACCCAAAGAATAGTCTTTCAAGTACATTGCCACCGTAGCTAGATGATTATTATCCTG
ACTATTAATTACTATTATGATTACTGTTGCCATGGTTTTTATGTTTTTCTGTGTGCCCAT
CCAATCCCACATCCAGCCACCACAGCCACTGCTGGGTTTT

The following amino acid sequence <SEQ ID NO. 224> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 90:

KPSSGCGGWMWDWMGTQKNIKTMATVIIIVINSQDNNHLATVAMYLKDYSLGVFFLMSMEQDDWAFEDIKE
TKGPDCNQRFHSHRPGFTWQHTFWTFFFFSGKETGSVENGRMRTNCRALPHSWTLSHSSRWGPPAHCWLCP
PQFLRIHTDFAKILRYVGHELWVCAHLVPSLYSTLHSSGVFLTAGATFHLHHYYIKWASIFPSEFQPLSGN
LTFFLVSFALRFCPFYCSNEFTQPSIPHESGQDPVTCDSHTDCVRVTPPVPGFPEPCLSRLTGQSWDMNWA
PELALFVSRSSRCLCRLPNPCSWAWVAESAGRLWCMH

The following DNA sequence Seq-2426 <SEQ ID NO. 91> was identified in *H. sapiens*:

TATTATGTTATTGTGTAATTATTTGAATTATTGTCCCCTTTCCATCAATCCCCCAAACAC
ACACATATTAGGTGGAAATCCTTAGGGGCTGAGATGATGTTTTATTTACATCTGCATGCC
TGATGTTAAGCCCAGTGCTGGGCACGAATGCGATTTAGTGAGTGTTTCTTGAACATGAAT
AATGAATTCACCAGTGAAAGCATGAGTGGATCTGGTGGGGGCACAAAAGGCTGACTCCAG
GTTCCAGGAATCTGGGTGGAGAAACTTCTGGGCTGGAGGGAGCAGAGGACCACTGTGTTA
GGTCTACGTGGTTCTGGCTGGCAGGGTTAGCAAGGATGCAGAGGAGTTTCTGGGTCTTGC
TCAAATGATAATTTAAAACAACAATAATAATTAACATTCATTTAGTTCTTACTATGTGTC
AGTCCCTTATTGCCTTCTATGTATTCAGCCACTAATCCTCAAAATTCTAGGGGTTAGATA
TTTTTCCGGTCTATACTATACATATGAGAAAAAGGGTAGAACAGGGAGGTGCAGAAACTT
GCCCCAGGATACACAGCAAGTAAAATGGGAACTGGGATTGGTCACCTAGGGATTCTTGTT
TTTTAGATTTTGTTTTTTTAATCTCTCTATAGCCCCTTAGGTTATTTATTGATATTTTTA
CTTTTTATTTTGAAATAATTGTAGATTCACAGGAAGTTACAAGAGAGAGGTCCTGTGTAC
TCTTCACCCAGATTTCTCCAATGCTTAGATTTTATATAACTGTAATACAATATGAAAACC
AGGAAACTGATATTGGTTCAATATATGTGTATACTTCTATGCCATTTCATCATGTGTAGA
TGTAACCACCATCATGACCAAGCTGCAGAACTGTTCCATCACCACGAAGATCTGCCACCT
GTTGCTCCTTTAAAGTCATACCAGCCCTCTTCCCTGTCCCCACCCACTGTCACTATGCTT
AACCCTTGGTAACCACTAATCTGTTTTCCCATCTCTATAG

The following amino acid sequence <SEQ ID NO. 225> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 91:

LCYCVIIIIVPFPSIPQTHTYVEILRGDDVLFTSACLMLSPVLGTNAIVFLEHEIHQKHEWIWWGHKRLTP
GSRNLGGETSGLEGAEDHCVRSTWFWLAGLARMQRSFWVLLKFKTTIIINIHLVLTMCQSLIAFYVFSHSS
KFGLDIFPVYTIHMRKRVEQGGAETCPRIHSKNGNWDWSPRDSCF<u>LDFVFLISLPLRLFIDIFTFYFEI</u>IV
DSQEVTRERSCVLFTQISPMLRFYITVIQYENQETDIGSIYVYTSMPFHHVMPPSPSCRTVPSPRRSATCC
SFKVIPALFPVPTHCHYAPLVTTNLFSHLY

The following DNA sequence Seq-2427 <SEQ ID NO. 92> was identified in *H. sapiens*:

TAGTTTCTCTGGTCTGCCTTGGGGAAGAAAGGAGAGCAGGAGAAAGAAAGGTGGGAGAAG
GCCAGAAAGACTTTGTTTCTGAAGCTCTTTCAGTTTCCTTCAGTTCAAAGCACTCATCAC
ACCAAGACACCATACTGTGGGGTATCACATTCTGAGCCCTAACACTTCCAATATTATGCT
ATGAATTTACATCATGATTTCAGGTAATTATTCCAACAATGCCACAAGGTGAGCATTTGT
GTTATCCAGTTTCACAGATGCAGAAACTGAAGTGGAAAAAATTGACTAGCATTATATGGC
TGGCAAGTGATCAAACAGGATTTTCTCATTATTTCATTCACTCAATAGTTATTGAGCTCA
TAATATATGCCAGGCATTATGTCAGACTTCATGGATACAGACAGGTACACAGTAAACAAG
GTGGCCACTGCCCAAATGGAGCTTGCATTCTGGTGGGGAAGACAGATAATAAACAACAAG
AAAGAAGCAATATAACAGATTGGGACAGTGCTATTAATATAAGTAAATGAAGGAGGGATA
TCATCAGGAGAATCTGGGAAGGAGTGGATGCTACCTGAGACAGGATGGTCAAGGATCTGC
CTAGTTGCAAAGCACTAGACTTTCCACAACCCCTTCTACCCTCCAGTGGGCCTCTGCAGT
ATATATGGCAACCAATTCTGGTTTCATGTATTCTACCACTTACTCCAACTCTAGTAAATA
TCTGCAAAGCTTACCATTGCCTACGACTCTCAGATTATTTCCCCAAGATGCTGCAGAATC
CTTATAATGTTTCTCAGCCTCAATAGAATGAAAAGCAGGTCTGTGCTTATATCACTTAAT
GACCAAAGAGGAAGGAAATTTACAATTAAAGTGTACTTTGCCAACTGTGGATGAATTAGT
TAGGTCACTGTGATCTACAGGTTAGATGTCTGTTCAGCAGTGTCCTCTACTTGAGATTCC
AAGGAGGTTGAAGCTCACTACTCGCCACCCCTCGCACCCC

The following amino acid sequence <SEQ ID NO. 226> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 92:

GARGGEASTSLESQVEDTAEQTSNLITVTLIHPQLAKYTLIVNFLPLWSLSDISTDLLFILLRLRNIIRIL
QHLGEIIESAMVSFADIYSWSKWNTNQNWLPYILQRPTGGKGLWKVCFATRQILDHPVSGSIHSFPDSPDD
IPPSFTY<u>INSTVPICYIASFLLFIICL</u>PHQNAS<u>SIWAVATLFTVYLSVSMKS</u>DIMPGIYYELNNYVNEIMR
KSCLITCQPYNASQFFPLQFLHLNWITQMLTLWHCWNNYLKSCKFIAYWKCGSECDTPQYGVLVVLTEGNK
SFRNKVFLAFSHLSFSCSPFFPKADQRN

The following DNA sequence Seq-2428 <SEQ ID NO. 93> was identified in *H. sapiens*:

ATCAGCGACACCATCCTGGTTGTCATCCCTGAGCTGTGTTAAGTAGGCACTTCCCCTAAG
AGAGTTAAAGGGGCACTCGTGAGATACTAAGAAGACTCCTTCCCCCAGCCCCAGGCCTCC
TTGTACCTTTTGCCTCTTCATTCTGTCTGCTGCCTTCTGGGAAATGATGGGACTGGCAGG
CTGTACTATGCAGCAGGGATAGCAGGGCTGTTTGCTCTGCCCTCAGGAAGGCAGATAACC
CCTAGAAACAGGAAGAGCCAAATGAGGTTGTGTAAGTCTGAGGCAGAAACATTAGTCGTG
AGAGCAAGACTTGCATTTGCAAGAGCCAGGCTGTGTGTGTGTTTGTGTGTGTGCGTGTGT
GTGTGTGCATGTGTGTGCACGTGTGTGCATGTGCGTGTGTGTGTCCGTGTGTGTGTGTGT
AAAACTGGATGGCCAAGAGCCAACCCCTGGAGGGCACGGAGACAGGGAAGAAAACAGAGT
GAAACAAAAATATTTGTGTAGAAGGCATAAAAGTTATCATCACAGACTCCACTGTGTAAA
GGCATAACTTGCTTTATTTATCTCTAGTGTATATGAACTTAGCCTCCCTTTCCATTCAGC

CTGTGAAAGGAGATAGTGCTTGGGCCATTTGGTAGAAGAAGGGGATGGGAGATGATCAAA
ACCCCAAGTAAGGTTCATATCCAATATAGTGTCTAAGCAGCAAATGACTAATGGCCGAAG
AAGGAGACTAGACAGAGGATTAGAGGCAGCCATGGGGCTGGTGCAGCTGTGGAGAGCTCT
GAGCAAAGAAACAAGGTTGGCAGGTGAGGAGGCCTAGGATAGAGGCCAGAAGGCCAAACC
TGGGGCTGTGCAGCCAGTGGTCATGGTGGCACAGCAGGCACTGGCTGGGCATTGGCTGGG
CATGCAGATGCCCAAGGCCAGCTGTGCCACATAGAAGCCCTGAGGAAGTGAGGGTAATTA
ACCCCTGAACAACCCAGATCATCTTCAGGGGAACAGCCAG

The following amino acid sequence <SEQ ID NO. 227> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 93:

GCSPEDDLGCSGVNYPHFLRASMWHSWPWASACPANAQPVPAVPPPLAAQPQVWPSGLYPRPPHLPTLFLC
SELSTAAPAPWLPLILCLVSFFGHSFAATLYWITLLGVLIISHPLLLPNGPSTISFHRLNGKGGVHIHRIK
QVMPLHSGVCDDNFYAFYTNIFVSLCFLPCLRALQGLALGHPVLHTHTRTHTRTCTHVHTHAHTHTHTHKH
THSLALANASLALTTNVSASDLHNLIWLFLFLGVICLPEGRANSPAIPAAYSLPVPSFPRRQQTERGKRYK
EAWGWGKESSYLTSAPLTLLGEVPTHSSGMTTRMVSL

The following DNA sequence Seq-2429 <SEQ ID NO. 94> was identified in *H. sapiens*:

CTGTGTTGGGTTCCTCCAGTGGTTTGTGGATGGAGATCATGGGGTGTGTTAGTCCATTTG
CATTGCTATAAAGGACTATCTGAGCCTAGGTAGTTTGTAATGAAAAGAGGTTTATTTGGC
TCAGGGTTCAGCAGGCTGTACAGGAAGCATGGCCCTGGCATCTGCTTGGCTTCCGGTGAG
GCCCCAGGAAGCTTCCAATCATGGCAGAAGGTAAACGGGAACCAGCATGTTACATGGCAA
GAGGGAAAGCAAGAGATGGGGGAAGGTACCAGGCCCTTTTAAACAATCACATCTCACATG
AACTCTTTTCTTTCTTTCTTTTTTTTTTTTTTTTTTTGAAATGGAGTCTTGCTCTGTCAC
CCAGGCTAGAGTGCAGCGGCACAGTCTT

The following amino acid sequence <SEQ ID NO. 228> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 94:

DCAAALPGQSKTPFQKKKKKKERKEFMDVIVKGLVPSPISCFPSCHVTCWFPFTFCHDWKLPGASPEAKQ
MPGPCFLYSLLNPEPNKPLFITNYLGSDSPLQCKWTNTPHDLHPQTTGGTQH

The following DNA sequence Seq-2430 <SEQ ID NO. 95> was identified in *H. sapiens*:

ATGTTAAAATAAATATTCATATATGCAACGGCAGGACTTTAAAAAATACACACAAATAGG
AAAACAAAAGAGACCATTCCAGAAGTCAACAAGAAAAATAAGTTTAGTTTTACAAGAAGT
TCACGATCTCGTCCTTATTTTACCACGTGCTAGAATTTGGTGACCAAAGTACCAGAACAT
TAGTTTGTAGAATAGTAATTTTTAAACTAAATTTTAGCAACAGAACATTAAAAAAAAATT
ATCTGGCAGCTGAATACAAAACGCAACAACAAAAACCAAAACACAAATGGAGCTACTCTA
GTTAGAGTCAGAGAGGCAGATCTCTGAACCATGCCTGCCTGCACACAACTCAAAAAACTA
GTAATGTAGAGTGATTTCTCAAGCCTCTTCTGGTATGCTAAACATTACAGATTCTTCTGA
CTAAAAAGAGAGGCAATCCCTGAGACTCTCCATAGAAACCCCAGGCTCTGTAGAAGCCAT
GAACATTTGGTATTGAGGGTGGAGGCAACAGAGTCTCCAGCTGTAGTTTTGTTTTGAACG
AATCTGGAAAATAAACTGAAAAACAATTTAAAACAAAAAGACTTTTAAATAGTAAATGTA
AAGTTGATGTGAGATGTTGGAATAAAAATGAAGGCCATTTCAAAACCCACCACAGGCAGA
TG

The following amino acid sequence <SEQ ID NO. 229> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 95:

SACGGFNGLHFYSNISHQLYIYYLKVFLFIVFQFIFQIRSKQNYSWRLCCLHPQYQMFMASTEPGVSMESL
RDCLSFSEESVMFSIPEEAEITLHYFFELCAGRHGSEICLSDSNSSSICVLVFVVAFCIQLPDNFFLMFCC
NLVKLLFYKLMFWYFGHQILARGKIRTRSTSCKTKLIFLVDFWNGLFCFPICVYFLKSCRCIYEYLFH

The following DNA sequence Seq-2431 <SEQ ID NO. 96> was identified in *H. sapiens*:

CCTGCAAAGTCTCTTCCTGCTGCACCTTCCTTCTGAAACCATTAATCACCACGACCCACT
GAATGAAGCCCAATCTCAAATCACAGTGAAAAATCCTGCAACGTGCAGGGTGATGAGTGT
TTACATTAGCTGAAATGAAATGATGTAATACCCAGAATCGAGGGAGGGCTGCGATCCAGA
GTCAGGGCATTGCAAAAACCTCTGTGAAACATAACTTTTCTACATTACAAAAAAATGTCC
TTGCGTTTTAGTAATCTGGCTTCTGTAAATTTAGGATTACTTGGATTTTTCTGATCTCAT
CAATTTGTTTTCCAAATAGAAATTCAGAACTTCCCAATTACTCACTGTTTTAGTCAAGTT
TAAAAAAAAGGGTAGCAAATAGAACCCAAAGTGTATACATGTGCAAAGAACCCAGTATCA
AGGGAATAATAATAGAAGGCAGCCATCCAGGTATGTGGGCACCTGCCATGCTGCAGAATA
GCAGAGCCTCCCAAGGGTCTAAGTGCCTTCAAAGTAAAGACAACTCCTAAGAAAGACAGT
ATTTGTTTAAGCCAGTGGCCAATTTTTCTTCCTATAACTGATGATGAACAAGAAAACCCA
GGAGTTCCTAGCCCTATTATTGATGGGCAACTGCTATTGATTAC

The following amino acid sequence <SEQ ID NO. 230> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 96:

VINSSCPSIIGLGTPGFSCSSSVIGRKIGHWLKQILSFLGVVFTLKALRPLGGSAILQHGRCPHTWMAAFY
YYSLDTGFFAHVYTLGSICYPFFTLKQVIGKFISIWKTNDQKNPSNPKFTEARLLKRKDIFLCRKVMFHRG
FCNALTLDRSPPSILGITSFHFSCKHSSPCTLQDFSLFEIGLHSVGRGDWFQKEGAAGRDFA

The following DNA sequence Seq-2432 <SEQ ID NO. 97> was identified in *H. sapiens*:

ACAAGGTCGGTGTACACCCCCTGTGATTCTGGGAGTAATATCTTCTCCTCCCTTGGATAT
TAGGAACAATATCACGGCGGGGGTGGGGGTTGTGTACAGCCTCTGCAATATTGGGAGTAA
TATCATCCTTTCTCCCCACTGGATATTAGGAACAATATCACAGGAGGTCTGGACACCCCC
TGCGATATTGGGAGTAACATCATTTTCTTTTCCCAGTGGATATTAGGAACAATATTGCAT
TGGGGTGTACACCCCTTCCGACATTAGGAGTAATATCATCCTCTCCCACAGTGGATATTA
GGAACAATATCTCAGAAGGAGTGTAGAACCCCTGCGGTATTAGGAGTAATATCATCCTCT
CCCTCCCTGGATATTAGGAACAATAACACAGGGAGAGTATACAGCCCCTGTGATATTGAG
AGTAATATAATCCTCTCCCCATCTGAATATTAGGAACAATATCAGGGGGGTGGGGTACAC
CATTTGCGATAGTGGGAGGAATATCATCCTCTCCCCACCTGGATATTAGGAACAATATCA
CAAGTGGAGTATACACCCCCTGCGATATTGGGAGTAATATCT

The following amino acid sequence <SEQ ID NO. 231> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 97:

QGRCTPPVILGVISSPPLDIRNNITAGVGVVYSLCNIGSNIILSPHWILGTISQEVWTPPAILGVTSFSFP
SGYEQYCIGVYTPSDIRSNIILSHSGYEQYLRRSVEPLRYEYHPLPPWILGTITQGEYTAPVILRVISSPH
LNIRNNIRGVGYTICDSGRNIILSPPGYEQYHKWSIHPLRYWEY

The following DNA sequence Seq-2433 SEQ ID NO. 98> was identified in *H. sapiens*:

TATTTAATCATATAATACTAAATATACTGTATTCAGAAGTTTTTGTGTTTTAGTCAGGT
AAGATGCAGGGTGTAGAGGTGTTAACCTTTCCTTAAAATTTTAATGGCTAGATATCTTGA
GATCTGTCTGATGTAGGAGTGGAAAGTGGGTGGTTCTTTTCTTCCCCATCATAAAGGCTC

ACAGCTGATACCCCTATAAAGAAAGACTGGTTAACAAGAGAAAAGCACAACAAATTTATG
AATGTGAATAAGTATGAGAGCCATACAAAAATATGAAAATTCAAAGAAATGGTTAGACGA
TTGATGCTTAACTACCTTCTTCATTAGGGAGAGGAAAGTTGGGGCGGGAGTGGGGGAGTG
GGGAATGGGGCCCCCTCCATCTCCAGGAGTGGATAATGGTTTGTAAATAATTCTGTTTGG
ACACTGAATGGAGCGGAATGGAAAGGACAAACAATAGGAATGTGAGGGGTGGAACTGCAT
GGTGAACAAAGGTTGTCTTATT

The following amino acid sequence <SEQ ID NO. 232> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 98:

DNLCSPCSSTPHIPIVCPFHSAPFSVQTELFTNHYPLLEMEGAPFPTPPLPPQLSSPRRLSINRLTISLNF
HIFVWLSYLFTFINLLCFSLVNQSFFIGVSAVSLYDGEEKNHPLSTPTSDRSQDIPLKFGKVNTSTPCILP
DNTKNFIQYIYYMIK

The following DNA sequence Seq-2434 <SEQ ID NO. 99> was identified in *H. sapiens*:

CCGAAGCCGAAAAGTCTGAAACTGGCCCAAAGTGGGAATTTATATCCCTGTTCTCCTGCT
GGAATGTTGCCTTTTCCTAAACCACCCATGGTCCCGCCCTACACCATCCTGTACCTATAC
AAACCCCATACTCAGCCAGTAGACAGGACTATGGTTGGACATTGGAGAGAAGCAGCTTGA
TGGCTTAACACCGAAGAAAAATCCAGCCAGAGACGGCCAGAACTTCCGGGGAGGGTTACG
CTACCGACCCTGTCTCCTTCTCAGCTCCCCTTCCTGCCGAGAGCCACGTTTCATTCACAA
TAAAATCCCCCACATCCACCACCCTTCAATTTATTCGTGCAACCTCATTTTTCCTGGCTG
GTGGACAAGAGCGCGGGAGCCACAGGTGGAGATACAAAAAGCTGTCACATTGGCCCTTTG
CCCTTGCTGGCGGAGGGCAGCCGCCTCACACAGAGGCAGAGGGCCCACTGAACTGTTAAC
ACTTAAGCCATCTGCAGATGGCAGAGCAAAAACAGCACTGGAACATGCCCTCTGGGGCTT
C

The following amino acid sequence <SEQ ID NO. 233> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 99:

RSRKVNWPKVGIYIPVLLLECCLFLNHPWSRPTPSCTYTNPILSQTGLWLDIGEKQLDGLTPKKNPARDGQ
NFRGGLRYRPCLLLSSPSCREPRFIHNKIPHIHHPSIYSCNLIFPGWWTRAREPQVEIQKAVTLALCPCWR
RAAASHRGRGPTELLTLKPSADGRAKTALEHALWGF

The following DNA sequence Seq-2435 <SEQ ID NO. 100> was identified in *H. sapiens*:

ATAGAGACGAAGTTAAACACTTAATTTGCAAAACTACTGAGAAGTAAATTTCTTGTTCCA
AGGTAACTGGAGTAATTGCCAAATGCAGATAAATCCTCCCCCTGAGTAGGAAGCCCCACA
CTGTTTTGAAAACAATTCCTAGACTTTGCCCCTGTTGAAGCTGATTGAATGCTCAACCAC
AAGACTCCACTGTTGTTAGCTCTCGCTTACTGCTTTTAGGGGCGGAGTTAACACTTTTCA
AAAATCCGAGCTTCCCTAATAAATACAGGGATTTAGTGAAGATTTTGATTGTCTGGGGTT
GGCATTCCTGAGGACAGAATAATTTATTTTGCTCTAAGCAGGTGTGTTATGAGAACAGAG
GCTATGTTGATAAGAGATCCCTGGGAGCTGGTAATATATTATCTTCTGTAATTTCTTCCA
AAAATAGACTTAATGGAAAGAGGATGCATAATATACCCCCTCTCAAAGGAAGCGTTCCCC
AATACAACAGAAGCAGTCATTCTAAAAACAGCTTTATGGCTCTGCAGTCAATAACTCTAT
TTTCTCCCCTTTCACAACTTCCTTCCTTCTGCTATGTAAGAACTTATGTGAGGGCACACA
CACATTCACG

The following amino acid sequence <SEQ ID NO. 234> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 100:

IETKLNTFAKLLRSKFLVPRLELPNADKSSPVGSPTLFKQFLDFAPVEADMLNHKTPLLLALAYCFGRSHF
SKIRASLINTGIRFLSGVGIPEDRIIYFALSRCVMRTEAMLIRDPWELVIYYLLFLPKIDLMERGCIIYPL
SKEAFPNTTEAVILKTALWLCSQLYFLPFHNFLPSAMELMGHTHIH

The following DNA sequence Seq-2436 <SEQ ID NO. 101> was identified in *H. sapiens*:

AAAAAAAAAAACCCCCATGATATGGATATTGTTATCATTCCTTTTCTCACAAATGGTAAT
ATTGAAATTAATAGAGGTTGTATATCGTGTCCACAGTCACACAGTTAGAAAGCGTCAGAG
CCAGGGTTTGAACTCAAGTAGCCTAACTATAGAACCCATATTTTTAATCACTATACAGTA
TTTTACTATCTGTTCCATCAAAAGAAATCATTTTTCAGAGTGGAGATGATAGAACATACA
TGAGAACAAGAGTATTTAAATCCAAGATACCTGCAAAGCATCTAGACACTCTAGATTTAG
ACTTTTAGCTCCTTGGCCAAGATTAATTACCTTTCAGGAAAATAAAACTACATACCAATG
AGATCACTAGACCTCTCGCAATGATCTATGAAGAATAATGGGAACAGCTATCTGGGTATC
TAATGGGCTAGAGTCAGATAAATGGTTTCTCAATAGATTTCCAGAATAATGGGGAAATTT
GGTTTTGCATTAACAATAGGCTACGTATGTTATATTCATTCTAG

The following amino acid sequence <SEQ ID NO. 235> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 101:

KKKTPMIWILLSFLFSQMVILKLIEVVYRVHSHTVRKRQSQGLNSSSLTIEPIFLITIQYFTICSIKRNHF
SEWRNIHENKSIIQDTCKASRHSRFRLLAPWPRLITFQENKTTYQDHTSRNDLRIMGTAIWVSNGLESDKW
FLNRFPEWGNLVLHQATYVIFIL

The following DNA sequence Seq-2437 <SEQ ID NO. 102> was identified in *H. sapiens*:

TCCTTTCTCTCTTTCAATCGTGTGGAGAAAATAATTATCAGTTGGGAACCATCATTTTTC
TACTACCATGAATGCAAATGTACTTCCATGACCCATCTTCCTTTACGAATAAAGTTACAA
TATAAGAAATACCACTACACATATCTGAGTTTATCTTTTAACTGTCTTTTAGAGCCCATT
CTCTTCTGCCTTCCTAGAACCTCTACTATGGATTATCCCTTTACCATAGCATTGTCATTC
TCTTCCTTTTAATGCATTTGTTTCCCACTGATTTTTAAACATGATTGAGTCATTTTCATT
AGAGACTAAATAAACATCCTCATTACATGGTTCACTAGGACCACTCCCTCTTCAGTTGTG
TGGAGAACTAAGCTTTTAGAAAGAGACGTCCAAACTCAGTATCTCTATTTCTGCATGCCA
CACAAATCCAGTTTGATTTTCATCCTCATCAGTCTACTAAAAGATGTCACTAAGGACACC
AATGAATTCCAAAAAAGCCCCTGAAATCCAATGGAAATTTGACATTTTTGACCACTTTCT
CTTTCTTCAAACATTCTTCCCTTAGTTTTCCAAGATAGTTTTCTTCTTTCCTTTCTACTC
ACTCTATTTTGATCTTCTTTGAAAATTCATCCACCTCTACCCAGTCATAAAATGTTAAGA

AGTTGGACTGCATTCTGGTTCTCTCTGAAGTTTGCTTTTAGGCAAGTACCAGATGGATTG
TATTTTAGAAAAGATTTGTCTGGAACATTTCCTGATGTCATTATCCAGAGACAATGAGAC
AACTCATTTGCTTATGAGGTTTTTACTACAGCAATCTAGAGATGGAATTTCCAATGGAAA
TAAAAAAGGGTTTTTATAATTTCTATATTGACACTGGCAGCTCCGCCTTTTAAAAAATTA
GTTCCTTTTAATGAATGTATTTTGGGAGTAGATTATAGTGTATTTAGTAAATTGGCACTG
TGTTTAGA

The following amino acid sequence <SEQ ID NO. 237> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 103:

TQCQFTKYTIIYSQNTFIKRNFFKRRSCQCQYRNYKNPFLFPLEIPSLDCCSKNLISKVVSLSLDNDIRKC
SRQIFSKIQSIWYLPKSKLQREPECSPTAFSSSTQWISYMLNCHVCASLKCAFLFTEMRDVLFMIFSL

The following DNA sequence Seq-2439 <SEQ ID NO. 104> was identified in *H. sapiens*:

TCTCATTTTGAAAATGTAAGTGGATATCACTACTGCATTGCCTGGAAATCCCACGAGGAA
GATAATGCCATAAATAACAGGGAGGTAGTGCATCTTGAGTGGGATGTTTTCATCAGTGCA
ATTTCCAAAAGCAGCTGCATAATCGGGGAAATCAGAAGCATTTGCTAAATAGTCTAGTGG
CTCATTCATGGTTGTCTCCTTTCATCTTGCAAGAAAACAAGAGAGTTCAGTTTGGCAATA
TGAATCAAATGAGCAGTAACTCGCTGATAAAGGAAAACAGAAAACATTAATGATAGGGTA
ATAAAAACAAGGATCTACTTTTAAATGAAAATTATTCTAACATCCTAAATTTGCCACTTC
TCTCTCTTTAATCTCAAAAGAGACCCTGTGGAGAAGAAATTGAATTTCCAAGAAAATGAC
TATGAGGCAAGTTACTAAATGCATCTAATAAAAATATAAAAGTTAAATTACCATGAGAGT
TAAAATGAGGGATTGGGAGAAAAAAGCCACATGTCGCTTTGGAAAACAATTTGGCAAGGT
CACCATTTGGAGAAGCCATAGGGTATCGCCATTAGAGACTTAACAACAGGACCTACTATT
AACCAAGTGTGATGCATGCCACCATCACTTACTTCTACATGTCACAAAATACTGAAA

The following amino acid sequence <SEQ ID NO. 238> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 104:

FQYFVTCRSKWWHASHLVNSRSCCVSNGDTLWLLQMVTLPNCFPKRHVAFFSQSLILTLMVILLYFYMHLV
TCLIVIFLEIQFLLHRVSFEIKEREVANLGCNNFHLKVDPCFYYPIINVFCFPLSASYCSFDSYCQTELSC
FLARKETTMNEPLDYLANASDFPDYAAAFGNCTDENIPLKMHYLPVIYGIIFLVGFPGNAVVISTYIFKMR

The following DNA sequence Seq-2440 <SEQ ID NO. 105> was identified in *H. sapiens*:

CCACCTGCTGTCCTGCTAGACGTGGAAAGATTCGCAGCAACAGAGCAGGGAAAATGAGTC
AAATGGAGGCCAAAAATGAGAACTAAGAGATTTGTGAGAATATTCAAGCAAGGCAAGGAG
AAAATAAGAGAAGGAAAGTAAAATATAGCCACAAGCAAAAGTGGTAACAAAATGCTTGAT
ATGAAGTCCTATTTACCAGTGATAAGCCACATGGATAGTTAGTTATGAGCTTTTTTGTAA
TCAACAGGAAAAGGAAAATCACAATTTTCAAGATTCCCAGTGTCTCTAAGGTATAAAGCC
CAAGTAATTGGAGAGAAGCACAACTATTTGTGGAACTAAGATAAAAATGAATTGCCTCTA
GTCAGTTTTTGAAGAGCCACTTGTCCAGGGTCTCACAGCTGCTCGGCCAGAATTTGAACC
CCAACCACATAGTTCCAGAGCCCACATTCTCAGACATAGCCCCCAATACTGCCTCTGGGC
TGGAGCTGGTATTCTCAATAACTGTTTGTTGAGTGGATAGGTGAATCACCATT

The following amino acid sequence <SEQ ID NO. 239> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 105:

WFTYPLNKQLLRIPAPAQRQYWGLCLRMWALELCGWGSNSGRAAVRPWTSGSSKTDRQFIFILVPQIVVLL

SNYLGFIPRHWESKLFSFSCLQKSSLTIHVAYHWIGLHIKHFVTTFACGYILLSFSYFLLALLEYSHKSLS
SHFWPPFDSFSLLCCCESFHVQDSRW

The following DNA sequence Seq-2441 <SEQ ID NO. 106> was identified in *H. sapiens*:

TATCCACATAAATGTGCATTTTCTTTTGGGCCAAAATGAGGCAGAGGTGTCATGTGAATT
TTTCATTCCTTCACACAACGATAGTCTCTCACAAAACAAAGAACAAAAGGAAACATATGT
TCACAGTGGGAAGGATTATTACTCGATCATCTGTATAAGCATGGCCCAAGGAGCCTTTGC
CAACCTACTGGGGATGTCACATGTAAAAAGGTTTCTCCAAAAGGTTGGCAATATGATTTA
TTAAAGGAGTCAGATGACATGGGAGTTAAGGGCAGCAAACTTCATTGTGATGGAAAGGAT
CTAAGCTGCTCCAGCAAAATGAAAGGATTATGGTTCACCTGCCAACACTGTGCAATTTAT
GGATGAAACCTCAACCACGAAAAGTGAAACTTCTTTGTGTGTGTGTATGGGGTTGCGAGG
GGAGACATAGGAAAGGAAAGGCAGACAGACCGTGGAAAACAGATATTTCCCCTGGATAAG
AGTGGAATGGCCAGTCTCATAACACTCATGTATTATAGAATTAAATATAAACCTGTTTCA
GAAAGTACAATATTAAGACCCTTTTTAAATCTTGATATTCTTTGATGATATCTCT

The following amino acid sequence <SEQ ID NO. 240> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 106:

STMCIFFWAKMRQRCHVNFSFLHTTIVSHKTKNKRKHMFTVGRIITRSSVAWPKEPLPTYWGCHMKGFSKR
LAIFIKGVRHGSGQQTSLWKGSKLLQQNERIMVHLPTLCNLWMKPQPRKVKLLCVCVWGCEGRHRKGKADR
PWKTDISPGEWNGQSHNTHVLNITCFRKYNIKTLFKSYSLMIS

The following DNA sequence Seq-2442 <SEQ ID NO. 107> was identified in *H. sapiens*:

TTTCCTACTGATCAGAGTTACTGTAGAATTTGATTTAGGTGTGTAAATTAGTCTGAGGCA
CACATTCAGTCTTAGGCAACCCTCTCTGTGATGGCATGCCTCAAAGCAGTGGTTTGAATT
AGGGGCAACCTTCAACCCTGAGGGACACTTGGCAACATCTTGAAATATTTCAATGGTCTT
AAGTGAGAAAGTGCTATTGGCATCTGGTAGATTCAAGCCAGGGATGATGCCAAAGATTTG
ACAAAACACAGAACAGGCCATACAACAGAGAATTATCTGGTCCAAAATGTCAATGGTGCC
ATGGTTGACAAAACCTGAGATAAGCTTAGGGAAGGATCCAGCACAGAGCAGAATGTATTC
TCTCTGTAAAGAAGCCAATCCCAAAGAGAAAGAAGTTGAGTAATGCTGCGTATATTTACT
CACTTTCTCTTTCCAAATTTCTTAGTTTGATAATTCACTCGACTTGCCCTGGTAAGGAAT
GAGGGAGGAAGCAAAAAAGACCAAGCTTGTGTTACACTAATTACTGTCCCTCAACAGAAA
AACGTGAGGTGAGGGGTAAGAAAGTCCCCCCATTCTCACATCTATATCCAATACAT

The following amino acid sequence <SEQ ID NO. 241> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 107:

VLDIDVRMGGLSYPSPHVFLLRDSNCNTSLVFFASSLIPYQGKSSELSNEIWKEKVSKYTQHYSTSFSLGL
ASLQREYILLCAGSFPKLISGFVNHGTIDILDQIILCCMACSVFCQIFGIIPGLNLPDANSTFSLKTIEIF
QDVAKCPSGLKVAPNSNHCFEACHHREGCLRLNVCLRLIYTPKSNSTVTLISRK

The following DNA sequence Seq-2443 SEQ ID NO. 108> was identified in *H. sapiens*:

TTTGCTCTTTTTCCTATGTTCATCATCTCATTGAATGGCACCCCCATCTGCATGGTAGCC
TGGGAAATATATTAAGGTATTATCCTTGAACCTTCTTTCTTTATCATCCCTATGTCCAGG
TAATCTGAAATTCTGTCAGAATATGCATCTTTAATCTATCTTAAACTGGCCCATTTTTAA
AAATTTCTATCTATCTTGACCTTACTTTACCTAAATGATTATCACTCTCCTAATTGTTTC
CTAATGGGCCTCATAGGCAAGACAAATCTGTTCCTTATACTGCCTCTAGAATTATCTTTT

CAAACACGGATGTGGCCATCCTTCTTTCTTACAAATGACCTCATAGTCCCAAAGACAAAG
TCTATACTCTCCCTAAATAACATTCAAGGCCCTCACTCACGCAGCTCCCTGATTCCCACG
TCAGTATTTTTGTCCTCCTCCCCTTCCCAAAGCACACTCTCACATACGCGTTATTCTACC
TGGAGTCATATTAAGCTACTTTCAATTCTGGGCTTTCTCTTAGCCTTCAACCCTCTCTTA
GGCTGGTGCATTCCTGGGGAGTGGTCCAATCCATGCACGTGCTACCATGCACCCACCTTT
CTT

The following amino acid sequence <SEQ ID NO. 242> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 108:

FALFPMFIISLNGTPICMVAWEIYGIILEPSFFIIPMSRSEILSEYASLIYLKLAHFKFLSILTLLYLNDY
HSPNCFLMGLIGKTNLFLILPLELSFQTRMWPSFFLTNDLIVPKTKSILSLNNIQGPHSRSSLIPTSVFLS
SSPSQSTLSHTRYSTWSHIKLLSILGFLLAFNPLLGWCIPGEWSNPCTCYHAPTFL

The following DNA sequence Seq-2444 <SEQ ID NO. 109> was identified in *H. sapiens*:

CTGCATGTTGTCTATTGGTCTGATCCATGGGTTGCTTTGCTCCAAGGTCCAGGCTAAAG
GAGATGCCCTCTCTTGGGGAATGTCATGCCCCTGCTAGAGGTAGTCTCTGCTTGGACTGG
GCACACTGCTACTTCGCTGCTCATTTCATCAACCCCAGCCAGCCACTGTGGGGCAAGCCA
GTGTTCCTTGCTTGTCAGAGATGCTGTACTTTGCATACAATGGTGAAGAGAGTGAACAGC
AGGGTGTAATTAAACAGTCAACCACAACCTGAAGCCACTTTCCCTGCTAAGTGGACCTCA
ACTCAATGGTCTCATTCTGAAAGATGTGGCCTAAATTCTTGCTTGGAATGGTAATTCCTC
TCTAATAGACTCTGCTGTTCTCTTGCCAGTCAAGAGGACTGAAGGGGATTGAAGGTCTGA
ACCTAGGCTCAGTGGCTACTGCCCCTCCTCCACAGCCGCTGGCTTCCAGCAGACATTCCT
GATGCTGATGTGCTCCTTGGAGTGCTGAGCTTTGGGGGAAATCCTGTTGCATGGTGCCAG
ACCCTCCTTCCCCATCTCATAACTCCATCACAGAG

The following amino acid sequence <SEQ ID NO. 243> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 109:

LCDGVMRWGRRVWHHATGFPPKLSTPRSTSASGMSAGSQRLWRRGSSHAVQTFNPLQSSLAREQQSLLERN
YHSKQEFRPHLSEDHVEVHLAGKVASGCGLFNYTLLFTLFTIVCKVQHLQARNTGLPHSGWLGLMKAAKQC
AQSKQRLPLAGAHSPREGISFSLDLGAKATHGSDQTTC

The following DNA sequence Seq-2445 <SEQ ID NO. 110> was identified in *H. sapiens*:

TTGTGGAGCAGTTAGAGACACATGGCAGTGTCCTTGAGTGGCTCTGAGTGTGGGACCATT
TTCTAGGTGATCACTCAGCATAGCTTACCGATCAGACTCAAGTGAATGGAACCTGCCCCTC
TTCCCTTTCCTCCTGGCTTTGGAACAGTTGCTACCAGGTGAGTGGTTTTTCCCTCCAGAC
AGTTACTGAGAGTAATCCCTGAGCACTCACTGGGTGCCTGTTCTGTGCTGACAGTCATCT
CATTCATCCTAACAGCAATTCCATTCTGCATCTTCTCTGGACACCCCCAGGACCATCCAG
GACAACCCTGCCTGACACCAGGCCTAGTGTGGCTCCATGATAACAAAGACGCAGGTCCAG
AGACAATCCCCCTACATGGTGCCTGCATCTGATTCCCCTTGG

The following amino acid sequence <SEQ ID NO. 244> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 110:

VEQLETHGSVLEWLVWDHFLGDHSALTDQTQVNGTCPLPFPPGFGTVATRVVFPSRQLLRVIPEHSLGACS
VLTVISFILTAIPFCIFSGHPQDHPGQPCLTPGLVWLHDNKDAGPETIPLHGACIFPL

The following DNA sequence Seq-2446 <SEQ ID NO. 111> was identified in

H. sapiens:

TCTTGCACTCTGGGCCCCCAAACAAGAGGCCACTCAGAAATCACAGTTTGAGAACAAGGC
ACCATTGCCCCCTGAGCCTGGGCTTTCCTGAGGCTTGGGTAAGAGAAAGAGAGATGAGAA
GGCTCCCTGGGCTACAGAGGTCTGGAGAGAAGCTGGCACCTGGGAAGAACAATTTCCCCA
GCAGCTAGCCAAGCTGGGGTCTTCCAAGTGGATGCAGAGACCTGCCCTGCTGCCCTCCCC
ATCCTCTGAGAGTGCCTTCTCTGGGCTTTTGCTTCAAAGAGCCATCTTTTTCCACATGGC
ACTCATCTTCCTTGTCCTTTGCTTCATGACACCTTGAGCGTGTTAGAAGCTAATCCTGAA
CAAGCATAGAAGGGGCACTTGGGGTAGGAGCTGCAGTGGCACCACCCGAGAGGCCAGCTT
TACCTCCCCCAAAGATCCACTGCCCAGAAGGGAAGACCAGGGGCCTCCCTGGTGCCAAGG
GCTTGAGAGTATGCATCCAATGCAGCTAGGTCCTCCACACACTGTGGTGGGGCCCCTCAC
CCTCAGATCAGCATCTTACTCTCA

The following amino acid sequence <SEQ ID NO. 245> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 111:

ESKMLIGGAPPQCVEDLAALDAYSQALGTREAPGLPFWAVDLWGRSWPLGWCHCSSYPKCPFYACSGLASN
TLKVSSKGQGRVPCGKRWLFEAKAQRRHSQRMGRAAGQVSASTWKTPAWLAAGEIVLPRCQLLSRPLPREP
SHLSFSYPSLRKAQAQGAMVPCSQTVISEWPLVWGPRVQ

The following DNA sequence Seq-2447 <SEQ ID NO. 112> was identified in *H. sapiens*:

TAACAAAACACTTTTTATCATATATGAAACTCCTGTACAATGATTTGGCTAGAAGAAAAA
AATAGTTGGAAGGTCAAATTTGTTTTAAAACATCTGTTCAAAAGCCTGCATTAAACTTTT
ATCTGTCCTGACAAAACATGTCTCAATTTCTTTCTAAAGCAGCTCTATTGTCCTAGCATA
TGCCTCACCAAGTTCTTTAAAGGGCATTTCCAACCTTAGTTCTGACAATGAAGACACAAA
GTAGGTTAGGTTCCAAAACCACCCTTCCTAGCCCTCCCTGTAGAAAATACCATGTTGCAC
AGTTACATGTGTCCCCTGACACAAACGACACTCATTTTACGTAGGTCACTGGACCTCAAA
CTGTTGTTGCTTGCTGTCCCAGCCAATTCAAGAGTGAAGGAAGATGTAACCAGACATACA
TATCTCCCTTTCT

The following amino acid sequence <SEQ ID NO. 246> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 112:

QNTFYHINSCTMIWLEEKNSWKVKFVLKHLFKSLHTFICPDKTCLNFFLKQLYCPSICLTKFFKGHFQPFQ
RHKVGVPKPPFLALPVENTMLHSYMCPLTQTTLILRRSLDLKLLLLAVPANSRVKEDVTRHTYLPF

The following DNA sequence Seq-2448 <SEQ ID NO. 113> was identified in *H. sapiens*:

CAGTCCAATGCTCCAGTTTTATAGATTGGGAAAACTGAGAGCCTAAGGGGTCACTTGTTA
TAGCTCCTATCCCCAAACTTACAAAACAAAGAGTTTTACAGAATGAGTCAAATATAATTT
GTTTGGGCTACTATTTCATTTTACCATTTTATCCCTATTAGTATTTATCACCATACATTC
AAAGGAATTCATACATGTAGACACATCTGAGGTGTTCCTGATTTCTCCTGTTCGACCTGT
GGTAAAACTCCTGTGGCACTATAGCACCTTTAGCTTATCAGTCTTCTTTCCCTCACCTCA
TAGATCAGAACTTATCAGCCCCCATCCTGGTCCTTCTGAATCTTTTGTCAAGTCATTGCT
TTCCAATCTCTGATAAAGTGTTGAAAGGGTACCATTATGCCTCTCAGAGATACACACAGT
CATGTGCCACCTAACTATGTTTCAGTCAGTGAGGGACCATA

The following amino acid sequence <SEQ ID NO. 247> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 113:

SPMLQFYRLGKLRAGVTCYSSYPQTYKTKSFTEVKYNLFGLLFHFTILSLLVFITIHSKEFIHVDTSEVFL
ISPVRPVVKLLWHYSTFSLSVFFPSPHRSELISPHPGPSESFVKSLLSNLSVERVPLCLSEIHTVMCHLTM
FQSVRDH

The following DNA sequence Seq-2449 <SEQ ID NO. 114> was identified in *H. sapiens*:

CCAATACCACCATCTGAGGGTCTAGAGAAGGCTTGATTTACTTTCATGAGTCCCGGAATA
AGATCTCCTCAAACAAGGAATTTTTTTTAATCATGGAAGTATGGCAATGGGCAACTAAA
CCAAAAGTCTCAGTGCTCCTCTCAGATATAGCTTCGCTCAGAAACAGGCAGCCTGGGTAG
AGAGATGGAATGTAAAGTCTTATTAAATGCTCAGCTGAAGTGTCAAGTAGGGGGCTTTGG
TGCTGTCCTTCAGGATGTAATATATGTACTAAACCAGTGACCGAATACTATACAGAATCA
GTAGTACCTAAAATACATGGATTTTTATACCAAGGCTTAGACATAGAATCAGCACTTGTA
ACTATCAAATGGTTGAGGAATTTCTACTTCATTTGTCCACAATTACGCTGGATTAGAAGT
GTTTGCATCCTTGCATCTGTGTGT

The following amino acid sequence <SEQ ID NO. 248> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 114:

PIPPSEGLEKAFTFMSPGIRSPQTRNFFLIMEVWQWATKPKVSVLLSDIASLRNRQPGRDGMSLIKCSAEV
SSRGLWCCPSGCNICTKPVTEYYTESVVPKIHGFLYQGLDIESALVTIKWLRNFYFICPQLRWIRSVCILA
SVC

The following DNA sequence Seq-2450 <SEQ ID NO. 115> was identified in *H. sapiens*:

TTTGTTACAATATTAAAAGTGTGTCCAAGGTCCAGAGATAGCATGTAACACTAACAAATT
CTGTGGGATGGTGGTGATGTCAATACCAAGAAAAGCTTTGCAGAGAGCTTGGGGTTTCAG
CCAAGACTCCACAAAGGCATAGGGGCTTTGTGGGAGAATGGCAGTCCTCCTGGAGAAGTG
GCAGATAAAAAGGTAAAGATCTGTGAGCAACGTCATCTTGAGTTCAGGAATTGACAATAG
TTTGGTATTAGAAGAAGAGTAAGAGTGTCAAAAGGAGCATTTGTGTAATCTTTCACTCCA
GAGATTTTAATCTCCTTAATAGAAAGTTGTTTGTATTGATTGAATGATTAACCTTTATTA
AGAATTTTGTTGTCTCAGGCACTGGATTAGTAGCTTTACACATTTCATTTAAATCTCACA
TTTTGATAGCTTCTACTATGGTTATTATTTTACAGAAGAAACTGAAGTTAAGA

The following amino acid sequence <SEQ ID NO. 249> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 115:

LTSVSSVKPKLSKCEIMKCVKLLIQCLRQQNSRLIIQSIQTTFYGDNLWSERLHKCSFHSYSSSNTKLLSI
PELKMTLLTDLYLFICHFSRRTAILPQSPYAFVESWLKPQALCKAFLGIDITTIPQNLLVLHAISGPWTHF
YCNK

The following DNA sequence Seq-2451 <SEQ ID NO. 116> was identified in *H. sapiens*:

CCTGAAACCATGGGCTCTTCGTACCTCCAGTGCCGCTCACATCTTATGACACATAGTAGG
GGCGTTAATAAATGCTTATTAAGTTGACGACTATGCCAGAAAAAGGGTGAGGGATTACAC
AAAGTTTTAACAAAATCTCACGGTAACTCTTCAGAAGCAAAAATAAAATAATAACATTTA
ATAAAAGTGCCTGCTCAAGGCCTGCAGCCCAATTCCAGGTTTGCTCCAAATGTTGATGGC
CTTGAGCTTTCTTGTGTGAAA

The following amino acid sequence <SEQ ID NO. 250> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 116:

FTQESSRPSTFGANLELGCRPAGTFIKCYYFIFASEELPDFVKTLCNPSPFFWHSRQLNKHLLTPLLCVIR
CERHWRYEEPMVS

The following DNA sequence Seq-2452 <SEQ ID NO. 117> was identified in *H. sapiens*:

CTGCTCCATGGGGATGGGCCTCAGTGAGTGTATGTGCCAGGCTTGAAATGGCTTCACGGT
ATGGGTTGCAGGAGCACCATGAGGTTCATCTAATCTTTGCCTTCCTCTGCCAGCATGTGT
GCCATCTGCAATGTCTCACTGAGCACTGAGTGGGGCCTGCTATGTGGGCAGTATCCCTGC
CATCTTCATATCA

The following amino acid sequence <SEQ ID NO. 251> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 117:

APWGWASVSVCARLEMASRYGLQEHHEVHLIFAFLCQHVCHLQCLTEHVGPAMWAVSLPSSY

The following DNA sequence Seq-2453 SEQ ID NO. 118> was identified in *H. sapiens:*

ATCTCATTGGTATGTAGTTTTATTTTCCTGAAAGGTAATTAATCTTGGCCAAGGAGCTAA
AAGTCTAAATCTAGAGTGTCTAGATGCTTTGCAGGTATCTTGGATTTAAATACTCTTGTT
CTCATGTATGTTCTATCATCTCCACTCTGAAAAATGATTTCTTTTGATGGAACAGATAGG
AAAATACTGTATAGTGATTAAAAATATGGGTTCTATAGTTAGGCTACTTGAGTTCAAACC
CTGGCTCTGACGCTTTCTAACTGTGTGACTGTGGACACGATATACAACCTCTATTAATTT
CAATATTACCATTTGTGAGAAAAGGAATGATAACAATATCCATATCATGGTGGGTTCTTT
TTTT

The following amino acid sequence <SEQ ID NO. 252> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 118:

KKEPTMIWILLSFLFSQMVILKLIEVVYRVHSHTVRKRQSQGLNSSSLTIEPIFLITIQYFPICSIK
RNHFSEWRNIHENKSIIQDTCKASRHSRFRLLAPWPRLITFQENKTTYQD

The following DNA sequence Seq-2454 <SEQ ID NO. 119> was identified in *H. sapiens*:

AGAGATCTTTAAAATACTCAAAGAAAATTGTCACCTAGAATTTGATAACTCTTGAAAATA
TCTTGCAAAAATGAAGGCTAAATAAATGATTTTTTGACAAAGAAAAGCTGAAAAAATTTA
TTGTGAGCAGACCTGTACTACAAGAAAGGTTAAAAGAAGTTATTTAGGTAGAAAGAAAAT
GATATCAAATAAGCAGATCTACACAAAGGAATGAAGATCTTCAGAAATCGTAAAATTGTG
GGTAAATCTAAAAGCCATTTTAAAAATTTTGAGTCATCTTAAGATTATTGTCTATAGCAA
AGAAAAATGCTAGCAATTTGTTATGAGGTTTAAAATATGCAGAAGCAGAAGTAAATCATA
TAATGATAGCAACATGACAACTGGGGGAAAATGAAAGTCCACTGAAGAAATGCTTAATAA
ATGTT

The following amino acid sequence <SEQ ID NO. 253> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 119:

TFIKHFFSGLSFSPSCHVAIIIFTSASAYFKPHNKLLAFFFAIDNNLKMTQNFNGFIYPQFYDFRSSFLCV
DLLIYHFLSTITSFNLSCSTGLLTINFFSFSLSKNHLFSLHFCKIFSRVIKFVTIFFEYFKDL

The following DNA sequence Seq-2455 <SEQ ID NO. 120> was identified in

H. sapiens:

ACTTTCCTTTCCAGGCATTTCTTGATGTGGAAGAGATTTACTGAGTCTGATACCTTTAAA
GGTCTGACAAGAGACATTTGCTGCCTATGCCTTCTGTTCTCTTGGAGGAGTGCTACCAAT
AAGGCTTCGTCAACATAACAAGGCCACCTTAGCTAGACAGGCCTCTTCCTTTCTTCCTCT
CATAACCTGTCTTGCCACTAAACCTGAATTACCAGCACAACCTCTTTGGGGCCATGCTCT
GAGCCCACATTCTTTCTATAACCTCAAGTAGGTATATAAGCTTCTGCGCCTTATTGTCTT
CATTCTGAAGGCTCTTATGTACATGCATTAAACAAATTTGTATCTCCTATTAATGTGCCT
TTTGCGAGTTGATTTTTCAGTGAAACTTCAGAGGTCCAACGGCAGTAGCCCCTACCAAGT
TCAAGATGCTCCACTTAC

The following amino acid sequence <SEQ ID NO. 254> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 120:

TFLSRHFLMWKRFTESDTFKGLTRDICCLCLLFSWRSATNKASSTQGHLSTGLFLSSSHNLSCHTITSTTS
LGPCSEPTFFLPQVGIASAPYCLHSEGSYVHALNKFVSPINVPFASFFSETSEVQRQPLPSSRCSTY

The following DNA sequence Seq-2456 <SEQ ID NO. 121> was identified in *H. sapiens:*

GTGATGTAAGACTGGTGGACTTAAATTAATTTTTTAAAGGCATCATGGGATTTTGTATCG
GCTATCTCTGTATCTAGAAGATGTCAGACTCATGGAAGTTTTGTCCATTTTATTCCCTTT
GCTTATCCATTCTTTCTTGTTTACAGAAAGACTTAATTTTCTGTCTCATATCTCTGTCCT
TCTTGCCCCACTATTTTTCCCCCTTCTCCAAAAATCCCAGCCCCAAAAACAGTCTACATA
TTGTGAAAAAGATTTCTCAAACCACAAGGGTGATGTAACTTTAGGCCTGTGTTTTCTCTC
TCACACACACAAAATATTGGATATGAGTGAGATTTTAAAAAATTGGTTTTTAAATGTGAT
GAAAAGAGTGTCCTTTTCACCAGAACAAAACAACCCTTAATGCTGAAGCCTCCTTCCCGA
TATGGGTGGCTTCCAAATATGAAGAAATCTGTGCATTGGGCCACAGGCTCCAGACAAAGT
CT

The following amino acid sequence <SEQ ID NO. 255> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 121:

CKTGGLKLIFRHHGILYRLSLYLEDVRLMEVLSILFPLLIHSFLFTERLNFLSHISVLLAPLFFPLLQKSQ
PQKQSTYCEKDFSNHKGDVTLGLCFLSHTHKILDMSEILKNWFLNVMKRVSFSPEQNNPCSLLPDMGGFQI
RNLCIGPQAPDKV

The following DNA sequence Seq-2457 <SEQ ID NO. 122> was identified in *H. sapiens:*

CCTTGGCAGCTCCAACTTGAACATGTAAAGGGTGTATTCAACAGACAAGTGAGAGAAGGA
ACCTCACACAGCCTGAGTGGGCCTGAGATAGGCTGAGGGGCCTAAGCTTCAATTGCATAA
GCAGGGCTAGGTCACTCCAGTTACCAAAGACAGAAACAGATAGTCCAGAGCCGTCCAGGG
GATGCTAGCCACTGCCCAGGAGATGATCAGAGAACACACAACAGAAATCAGAAAATGTAG
TACAAGAAGAATTTGCTGATAGGTGCAATCGCCTCAGCAAGGCACAGGAAACTCAACTCA
GAAGGCAGTCTGTCTGTCATCCACCAATTCTCTGGGTCAAGTCTGATGTGCACTCATAAA
GTAAAAATGCACTGTTATTGTGACTGAGAAAAAAAATAAAGCTAAAAGGTAAGTGCCTAT
AAAATAAGATTTTACTAATGCAAACAAAAGCCCTAAAGAAGTGTGGTTTGAGCCCAGTGT
CCTCCTCTATTAGCACCAACAATGGATAGGTGGTTGAGTCTGTCAAAATGCCTCTGGGTT
TACAGAAATGAAAGCTTGGTCTGTGCCC

The following amino acid sequence <SEQ ID NO. 256> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 122:

GHRPSFHFCKPRGILTDSTTYPLLVLIEEDTGLKPHFFRAFVCISKILFYRHLPFSFIFFLSHNNSAFLLY
ECTSDLTQRIGGQTDCLLSVSCALLRRLHLSANSSCTTFSDFCCVFSDHLLGSGHPLDGSGLSVSVFGNWS
DLALLMQLKLRPLSLSQAHSGCVRFLLSLVCIHPLHVQVGAAK

The following DNA sequence Seq-2458 <SEQ ID NO. 123> was identified in *H. sapiens*:

CATTTTTTACCACATATACTATAAGAATTAGTATTATTTTTGATTAAAATAAATGTTATT
TTCAGAGGTGCAATTTTTTGCTTTCAGTAAGATTTCTAATTTAAGGAAGTCATTTTAAAG
GCTAAATTTAAATGAGAAAAAGAGCTTGTTGCACTTGTTGATCCAGTTGGATCCAGTTTT
CTCTGCTGGTCCATTTTTTGTATCCCTTTTGAGTTTGCATTCCTTTTTAACATTTTTTGG
TATAGCAGATTTTTATTTTTTGGTACATTTGTGCACATAAACTTCTTGGTGTGGAGGAGA
GGTTAAATTTTAATAGCTAATGGGACAAAGGTATATAGGGATATATAGGTACAACCCTAG
CTCTTATTCTTTCTTTTCCTCCATAGTATTCTGGTGATGTAGGGATAAAATTT

The following amino acid sequence <SEQ ID NO. 256> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 123:

HFLPHILELVLFLIKINVIFRGAIFCFQDFFKEVILKAKFKEKELVALVDPVGSSFLCWSIFCIPFEFAFL
FNIFWYSRFLFFGTFVHINFLVWRRGILIANGTKVYRDIVQPLLFFLFLHSILVMGN

The following DNA sequence Seq-2459 <SEQ ID NO. 124> was identified in *H. sapiens*:

CCAAGCAAAGTTATATTTGTATTTTATTTTACATTTATTTTGTTATATTCCTTTTATCTA
CTTAGGTTTCTTCTCTACTTCCCTTTTTAATTGAAGAGTTTAATGCATGTATCTGTGTGT
TTGCTTGAAAAAAAACACCAAGTATAACATGTTCTATCTATGAATACTTCTGGCCATTAA
CTCAAAAGGTACTATATTACAGACAGAAAAGCACCAGAAAGCAATCAGGGACTTCATCTA
AGAGGTAGGACAGCATAGTTGGTAAAAATACAGACCCTGGAGGCAAACTGCCTGGGCTTG
AATCCCAGCTTTATTACTTTGGGAAAACTACTTATCTTCTTTACTTGTTTTGGTATCCAT
GTCTGTGAAATGGAAGTAATAATAATCCTCTCATAGCATTGTTGTGAGGTTTCAATAGAT
GAAGTGAAGACTTTAGAAGGGCACATGATAAGAATTATATAAGGGTTACCTATTATTGCT
ATCCAATTTGTCATAGCAAGCTAAGGGACCTTGGGCAAGTTACTC

The following amino acid sequence <SEQ ID NO. 258> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 124:

KQSYICILFYIYFVIFLLSTVSSLLPFLIEEFNACICVFAKKTPSITCSIYEYFWPLTQKVLYYRQKSTRK
QSGTSSKRDSIVGKNTDPGGKLPGLESQLYYFGKTTYLLYLFWYPCLNGSNNNPLIALLGFNRSEDFRRAH
DKNYIRVTYYCYPICHSKLRDLGQVT

The following DNA sequence Seq-2460 <SEQ ID NO. 125> was identified in *H. sapiens*:

ACTGGTAGAATGGGCTCATTCAAGCATGTAACGCCCTTAAATTTTTCATTTAAATTTTCT
GTGCCTTAGAAATGAACTTTACAGTAATCTTTGCTTTCTAAAAATAAATGTGTTTCTTGT
TAAGCATTTAGTCTCATCACAAATTCTGTTTTAGAAAAAAACAACAGAAAATAGTGAATG
AGAAGGGTAGGAGACTTAGGACTCAGCGAATTCTATCTCAGTGCCAAGACTTTAAAACTG
GGAATAAATGCTACTTCTCCATGACCTGGGTCTGATAATTTGTCTGCAGGAACACTGTTT
CTAGAGGGTGGTGTGGTACAGTGGGAGGAATGGACTTTGGAGTGAGATCCATGTTCAAAT
CCCAAGTCACTTACCTTCTCTGATCCTCAGTTTCCTCATCTGTAAAATGACCATAATCAA
CACCATCTCGAAGATTTGTGGTGACAACACAGCATTTACTTCCTGCTGTATACTTCCCAT

TTCCTCTTGTAGAGACAGAATTTTCCACTTTATTTTAATCTATAATTATGTAATCCCATT
TAAAAATCACCCTTCGACTTTCAGTTCCACAAGGC

The following amino acid sequence <SEQ ID NO. 259> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 125:

LVEWAHSSMRPIFHLNFLCLRNELYSNLCFLKINVFLVKHLVSSQILFKKTTENSEEGETDSANSISVPRL
NWEMLLLHDLGLIICLQEHCFRVVWYSGRNGLWSEIHVQIPSHLPSLILSFLICKMTIINTISKICGDNTA
FTSCCILPISSCRDRIFHFILIYNYVIPFKNHPSTFSSTR

The following DNA sequence Seq-2461 <SEQ ID NO. 126> was identified in *H. sapiens*:

ATTGCTCTCTTCTAGATTTTCTAATGTTGGTCGGTGCCCTTCGTAAGTTGTGTACAAAGC
TGGATCCAGTACTCCAAGGGTGATCTGACCTCACAGAGCACAGTGCCTGGGGAGTGCCCT
TAATCTGGACTTGGAATTCCATCATACAGAGGCCAAGTCTCTGACCATGATGTTCTCTCT
GTGTAACTGGGGCTGCTGAAACCCAAGTATTGTCAGCCAGTGCCGGTCTCCAGCCATGCT
TGTGTCTTTTAAGAAGTGACAGTAACTGCTATTTGTGGAGATGGCTATTCATAGGGACTC
CTTTTCTTTGCCTGACAGAGGCCCAGTGTTCTAAGCTCTAAGAGGGGCTCTGATGCCAGC
ATGTGAGTCACACTCACTTGCTACTGTTCTTTTCCAGAGTTTTGGGCCACTTGTTGCTGC
ACATCACTACCTCCTCTCCCCCTGCCCAGCTTGCATTGTCGCCCTTCCCCATCTACCATG
CTGTCCTTGAACATAAGGCGCTTCTCTGCATTCCATGTGTCTACTTTGTAGTTATGTGCT
GCATTTTGAAAGAGCTGAATCTATGTCCAGGTTCAAGAAAGAATGCTGATCAACTGTTGG
CAATAGATGGGTTTAATATATCTTATGATTGGTTCTTG

The following amino acid sequence <SEQ ID NO. 260> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 126:

CSLLDFLMLVGALRKLCTKLDPVLQGSDLTEHSAWGVPLIWTWNSIIQRPSLPCSLCVTGAAETQVLSASA
GLQPCLCLLRSDSNCYLWRWLFIGTPFLCLTEAQCSKLEGLCQHVSHTHLLLFFSRVLGHLLLHITTSSPP
AQLALSPFPIYHAVLEHKALLCIPCVYFVVMCCILKELNLCPGSRKNADQLLAIDGFNISYDWFL

The following DNA sequence Seq-2462 <SEQ ID NO. 127> was identified in *H. sapiens*:

TAGTCTAGACTCTTTTTCCCCTTTTAAGGTCAGCTGATTAACCTTAATTCCATCTAATAC
CTTGATTTCCCTTTGCCATGTATGTCCTGGGGATGAGGATGTGGATGGATCTAGGGGGGC
CGGTATTCTGGCTACCATAGCTATCTTGCTCTTTTTGTTTATAATTATGATATGTTCCAA
AAAGGAGTAAAACGTAATACAAGAAGATAAAAATACATTTACCATTAAGTAAGAAAAAAG
ACAAGGGAGAAGAGAATAAGAAAATGAGTCAGGAGTGGGATTTATACAAAAAATTAGTGA
GTCCACTTTACTTCCTGGAAGTGGATGGTGAGCTTTTCTTGCCAGCCTTCTTGAAGAGGG
AAGCACTGTCAGTTATGTTGTAGTGTGTCGATCTAGTAAAATCCAACTGGTTGTTCAGAT
ACCTAGATGAATATTCTTGATAGGAAGATGAAAAAAAAATTTCTTCCAAAGTCTTCATGG
ATACATAAAGTGTATAATGAGCAAAACCTTTGACATGTTTACAGTAAACCCAATGGTGTG
TTTCACCTGGCCTTTCTCTTCTTTCGTTTACTG

The following amino acid sequence <SEQ ID NO. 261> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 127:

QTKEEKGQVKHTIGFTVNMSKVLLIIHFMYPRLWKKFFFHLPIKNIHLGITTSWILLDRHTTTLTVLPSSR
RLARKAHHPLPGSKVDSLIFCINPTPDSFSYSLLPCLFSYLMVNVFLSSCITFYSFLEHIIIINKKSKIAM
VARIPAPLDPSTSSSPGHTWQREIKVLDGIKVNQLTLKGEKESRL

The following DNA sequence Seq-2463 SEQ ID NO. 128> was identified in *H. sapiens*:

CATCTATTCGACGACCTTGAGTTACCGCTGAGACATTTCTGAGGCACAACACTAAGAAAA
CGCATGTAATTGTCAAGCGTGGCAGGGCAGTATTGCTCTCAAAGTCCCGTCTGACTGACA
GGGCAGAGGTTCTTCCTCACTGCCCGAATCTGCTTCCCGACAGCTCCAGGGTTCCCTCAG
GAAGCCGCCCTCCACCTTCACCTCAGGCATGTCCTGCAGAGCCCTCTGGAGAACCAGCTT
CAGGTTCTGCCTATTTTGACGCTGCCTAAAGGAGCCCACGAAGAAGTAAATGACGGGGTT
GGCACTACCGTTTAGAGGAGACAGGAAAATGGAAACTAGATGGACATGACAGAAAATGAC
TTCCAAATCCAGGTGTATCCCAGTAGACAGAGCCCACCGAATGCCGAAGGGCAGGCTGCG
GAGTAGGAAGACTAGCACTGTGAGCAGGATCGTCACGTACA

The following amino acid sequence <SEQ ID NO. 262> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 128:

YVTILLTVLVFLLRSLPFGIRWALSTGIHLDLEVIFCHVHLVSIFLSPLNGSANPVIYFFVGSFRQRQNRQ
NLKLVLQRALQDMPEVKVEGGFLREPWSCREADSGSEEEPLPCQSDGTLRAILPCHAQLHAFSCCASEMSQ
RLKVVEM

The following DNA sequence Seq-2464 <SEQ ID NO. 129> was identified in *H. sapiens*:

TCACTGGAGAAGCCTAGTCACCTGGGCAGAATATCTTGAACCTAGGATAAGTTCATCCAT
GGTAGACCAACTCTGTGATGGAGTTATGAGATGGGGAAGGAGGGTCTGGCACCATGCAAC
AGGATTTCCCCCAAAGCTCAGCACTCCAAGGAGCACATCAGCATCAGGAATGTCTGCTGG
AAGCCAGCGGCTGTGGAGGAGGGGCAGTAGCCACTGAGCCTAGGTTCAGAGCTTCAATCC
CCTTCAGTCCTCTTGACTGGCAAGAGAACAGCAGAGTCTATTAGAGAGGAATTACCATTC
CAAGCAAGAATTTAGGCCACATCTTTCAGAATGAGACCATTGAGTTGAGGTCCACTTAGC
AGGGAAAGTGGCTTCAGGTTGTGGTTGACTGTTTAATTACACCCTGCTGTTCACTCTCTT
CACCATTGTATGCAAAGTACAGCATCTCTGACAAGCAAGGAACACTGGCTTGCCCCACAG
TGGCTGGCTGGGGTTGATGAAATGAGCAACGAAGTAGCAGTGTGCCCAGTCCAAGCAGAG
ACTACCTCTAGCAGGGGCATGACATTCCCCAAGAGAGGGCATCTCCTTTAGCCTGGACCT
TGGAGCAAAAGCAACCCATGGATCAGACCAATAGACAACATGCAGCCCTCATCTA

The following amino acid sequence <SEQ ID NO. 263> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 129:

HWRSLVTWAEYLEPRISSSMVDQLCDGVMRWGRRVWHHATGFPPKLSTPRSTSASGMSAGSQRLWRRGSSH
AVQSFNPLQSSLAREQQSLLERNYHSKQEFRPHLSEDHVEVHLAGKVASGCGLFNYTLLFTLFTIVCKVQH
LQARNTGLPHSGWLGLMKATKQCAQSKQRLPLAGAHSPREGISFSLDLGAKATHGSDQTTCSPHL

The following DNA sequence Seq-2465 <SEQ ID NO. 130> was identified in *H. sapiens*:

AAGAGTTAGAGCAGGATTTTACCTTGTTTTACAAAAAAGAAAAGTTTATTTTGAAAAAAA
TTCCAACCTTGCCTCCTCCGAACTATAGTGAAAAGATAATTTTCCACATCCCTTTGTTCA
GGAAATGAGGACACAGTGGTGTCATTGGGTTTTGATTGTCCACTTGGAAAAGGTTAAAAC
CTGTCCTACAGTCATGATGACTTCAGTTCCATTTAAGTGGGGTCCTGTCTCTCTCACTCT
CCACCGACTGTACCTTTACTATAACATGGCCTTATATAGATAGCTTTGAGTAAGTGTGTG
TTAAATGACTGCCCAAGTGAATGGAAAATTGAGAAGGGCCTCCAGCACTGGAGTATGGAA
AGGAGCACTGGGTTCATTGACTCTTTGGATTTCTCCCTTGCTACGTAAGTCCGTTCCCTA
AAGGACATGGATCTTGACAGTGTTGGAATCTTCAGAAATAATTGCAATACCAGAAGTTAT
TTAAGATTTTACCATTTTCAAAGTATTTGTACGTAACACTTTCATATGTTTTTGTTTCCT

AGCTACCTCAGTTTCCCTGTTGGCTTGAGCAGATTAGTGTAAAGAGGTGGTGACATCAGG
GGAAACAGGTTTACTCAGCCATCTTCATTACCATATTATCACTGACTTGAGGCTCCT

The following amino acid sequence <SEQ ID NO. 264> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 130:

GASSQYGNEDGVNLFPLMSPPLYTNLLKPTGKLRLGNKNIKCYVQILKWNLKLLVLQLFLKIPTLSRSMSF
RERTYVAREKSKESMNPVLLSILQCWRPFSIFHSLGQSFNTHLLKAIYIRPCYSKGTVGGEERQDPTMELK
SSLDRFPFPSGQSKPNDTTVSSFPEQRDVENYLFTIVRRRQGWNFFQNKLFFFVKQGKILLL

The following DNA sequence Seq-2466 <SEQ ID NO. 131> was identified in *H. sapiens*:

TAGTCGCTGCTTTCTGTTTCCGCTTAAAGATGGAGATATTTTTTCCTTTCATGCTTGAGG
AGTCTCGAAAGTTTTGCACACTCTTCCACCTCCTGGAACTTCACTGTGCCATTCAGGGTG
ACTACTGCTGTCTGGCTCCACTCGAGGGAAGCCAGGTAACCTGTGTTAGGCCGCGCTTTT
CCTGGCGGCCTTGTAAATCTGTTAGTACATGAAAAGCATGACGCACATGGGGATTAGGAT
GCCAATGCGGTGGAGTAAATCGTGTAGCCAAAGTCTTGACTGACCAAGCACACCTTATCA
TCGTTTACATTCTGAGCCCGACCAAAAATGGTAGGTAAAGTGACAAAGGCGGAAAGAAGG
CAGACAGAAAGAATCATCTTCGTCATGCATTTCCCCTTCTGCCTCATAGGGTACGTGAGA
GGCTTCATGATCCCAAGGTACCTGTCGATGCTGATCACGTACAAGGTCAAGATCCAGGCC
GTGCAGCACATGACATTCACGGAGAAGACGTTACAGAAAAAGTGTCCAAAGATCCACTTG
CCCCCGATGAGGTCGGTGACACTGAT

The following amino acid sequence <SEQ ID NO. 265> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 131:

ISVTDLIGGKWIFGHFFCNVFSVNVMCCTAWILTLYVISIDRYLGIMKPLTYPMRQKGKCMTKMILSVCLL
SAFVTLPTIFGRAQNVNDDKVCLVSQDFGYTIYSTALASSPCASCFSCTNRFTRPPGKARPNTGYLASLEW
SQTAVVTLNGTVKFQEVEECAKLSRLLKHERKKYLHLAETESSD

The following DNA sequence Seq-2467 <SEQ ID NO. 132> was identified in *H. sapiens*:

AGTGTTACAGCTGGGCAGCCAGAGAGACAGCATGTAGTCCTCATTGAAGCAGAAAGACAG
AGGGTTCTGAGACAGAGGTCTCCAGGAAAAAAAAAAAGAACCTGACTTACTGGATAAACA
AGTCTTTAGTTTAAAAAACAACAAAAAACTGTATACACATATATATATAAAATCAGGTAG
TATAAAGAAAAACAGAACTCCAGAGATTCCTGGGTCACAGAAGGGGAAAGGGCTGTTCAA
GAAAGTGAAATTGAACTAACTGAAAATACAGCTATCTTTATATTGGAAGGACAGTCAGGA
AGTCAACAGATAAGGCCTAAACTGCATAAAGCAGGAAACAGCAGACTAAAGACATTATTA
AGAAATATGGAACACAACCAAAAGAAATAGCAAAAACAATGAAAAGTGACTGTTTTTCAT
AAGTGAGGCAGGGGAAGAGAAGGGGTTATTTTTTTCCCCATTATATGTCTTTAAGAACTA
CTTGCTAAAAATATTGGGCACATATGAATTTGATAAAAGCGAAAAACTTTTTACTTCACA
AGTGCAGCTTTAACATACGTTGATTACAGTGAAGT

The following amino acid sequence <SEQ ID NO. 266> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 132:

FTVINVCSCTCEVKSFSLLSNSYVPNIFSKFLKTYNGEKNNPFSSPASLMKNSHFSLFLLFLLVVFHISCL
SAVSCFMQFRPYLLTSLSFQYKDSCIFSFNFTFLNSPFPFCDPGISGVLFFFILPDFIYICVYSFLLFFKL
KTCLSSKSGSFFFSWRPLSQNPLSFCFNEDYMLSLWLPSCNT

The following DNA sequence Seq-2468 <SEQ ID NO. 133> was identified in

H. sapiens:

AAAGGTGACAGAGAAGTAGGTGAGGAATTCAGTTTTAAATTTATTCATTTTTAAGTTGTG
TCAGGTCTCCCCAAGATTATCCCTCGGTTCTGTGATTCATAGGACTTAGCATATAGTTGT
ATTCACAGCTATGACTTATTAACAGAGGGATACCGAAGCATAATCAGCAAAAGGAAAAGA
TGCATGAGGAAAAGTCTGAAGAAACCAGGGACAGCTTCCAAGATTCTTTTCCCAGTGAAA
TTACACAGGATATGCTTAATTCTTTCAGCAAGGAATTGTGACAAGACATGTGAAACACTA
CCTGCCAGGGAAGTTCCTTAGTGACTCAGTGCCCATGGTTATTATTGGGGACTGGTCACG
TATGCCCTCTTTGCCTCATACTTAGAGAATTCCAGTTCCAGAAGGAAAGCAGGTATTCAG
TATAAGCCATATTATTTGCATAGACCAGTTTAGGATCAAGGAATTGTAGGAAGCTTTTCA
AAATCTAAGACCCCAAATACCAGCCAAGAGCCAGCCTTGCAAGCAGGACATTTTAAGAGT
AGCAGTCTTGGGTCTGCTGTATTAACTCTTTTCTGCACAGAAATGATAGTATGACATCTA
AGTTATTATTATCAAGGGACCGAGAAATGCATGTTTTTAGGCTAGGGAAG

The following amino acid sequence <SEQ ID NO. 267> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 133:

FPSLKNMHFSVPLRCHTIISVQKRVNTADPRLLLLKCPACKAGSWLVFGVLDFEKLPTIPSTGLCKYGLYI
PAFLLELEFSKYEAKRAYVTSPQPWALSHGTSLAGSVSHVLSQFLAERIKHILCNFTGKRILEAVPGFFRL
FLMHLFLLLIMLRYPSVNKSLIQLYAKSYESQNRGIILGRPDTTKINLKLNSSPTSLSP

The following DNA sequence Seq-74 <SEQ ID NO. 134> was identified in *H. sapiens*:

ATGAACCAGACTTTGAATAGCAGTGGGACCGTGGA
GTCAGCCCTAAACTATTCCAGAGGGAGCACAGTGCACACGGCCTACCTGG
TGCTGAGCTCCCTGGCCATGTTCACCTGCCTGTGCGGGATGGCAGGCAAC
AGCATGGTGATCTGGCTGCTGGGCTTTCGAATGCACAGGAACCCCTTCTG
CATCTATATCCTCAACCTGGCGGCAGCCGACCTCCTCTTCCTCTTCAGCA
TGGCTTCCACGCTCAGCCTGGAAACCCAGCCCCTGGTCAATACCACTGAC
AAGGTCCACGAGCTGATGAAGAGACTGATGTACTTTGCCTACACAGTGGG
CCTGAGCCTGCTGACGGCCATCAGCACCCAGCGCTGTCTCTCTGTCCTCT
TCCCTATCTGGTTCAAGTGTCACCGGCCCAGGCACCTGTCAGCCTGGGTG
TGTGGCCTGCTGTGGACACTCTGTCTCCTGATGAACGGGTTGACCTCTTC
CTTCTGCAGCAAGTTCTTGAAATTCAATGAAGATCGGTGCTTCAGGGTGG
ACATGGTCCAGGCCGCCCTCATCATGGGGGTCTTAACCCCAGTGATGACT
CTGTCCAGCCTGACCCTCTTTGTCTGGGTGCGGAGGAGCTCCCAGCAGTG
GCGGCGGCAGCCCACACGGCTGTTCGTGGTGGTCCTGGCCTCTGTCCTGG
TGTTCCTCATCTGTTCCCTGCCTCTGAGCATCTACTGGTTTGTGCTCTAC
TGGTTGAGCCTGCCGCCCGAGATGCAGGTCCTGTGCTTCAGCTTGTCACG
CCTCTCCTCGTCCGTAAGCAGCAGCGCCAACCCCGTCATCTACTTCCTGG
TGGGCAGCCGGAGGAGCCACAGGCTGCCCACCAGGTCCCTGGGGACTGTG
CTCCAACAGGCGCTTCGCGAGGAGCCCGAGCTGGAAGGTGGGGAGACGCC
CACCGTGGGCACCAATGAGATGGGGGCT**TGA**

The following amino acid sequence <SEQ ID NO. 268> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 134:

MNQTLNSSGTVESALNYSRGSTVHTAYLVLSSLAMFTCLCGMAGNSMVIWLLGFRMHRNPFCIYILNLAAA
DLLFLFSMASTLSLETQPLVNTTDKVHELMKRLMYFAYTVGLSLLTAISTQRCLSVLFPIWFKCHRPRHLS
AWVCGLLWTLCLLMNGLTSSFCSKFLKFNEDRCFRVDMVQAALIMGVLTPVMTLSSLTLFVWVRRSSQQWR
RQPTRLFVVVLASVLVFLICSLPLSIYWFVLYWLSLPPEMQVLCFSLSRLSSSVSSSANPVIYFLVGSRRS
HRLPTRSLGTVLQQALREEPELEGGETPTVGTNEMGA

EXAMPLE 2: CLONING OF nGPCR-x

cDNAs may be sequenced directly using an AB1377 or ABI373A fluorescence-based sequencer (Perkin Elmer/Applied Biosystems Division, PE/ABD, Foster City, CA) and the ABI PRISM Ready Dye-Deoxy Terminator kit with Taq FS polymerase. Each ABI cycle sequencing reaction contains about 0.5μg of plasmid DNA. Cycle-sequencing is performed using an initial denaturation at 98°C for 1 min, followed by 50 cycles: 98°C for 30 sec, annealing at 50°C for 30 sec, and extension at 60°C for 4 min. Temperature cycles and times are controlled by a Perkin-Elmer 9600 thermocycler. Extension products are purified using Centriflex gel filtration (Advanced Genetic Technologies Corp., Gaithersburg, MD). Each reaction product is loaded by pipette onto the column, which is then centrifuged in a swinging bucket centrifuge (Sorvall model RT6000B table top centrifuge) at 1500 x g for 4 min at room temperature. Column-purified samples are dried under vacuum for about 40 min and then dissolved in 5μl of a DNA loading solution (83% deionized formamide, 8.3 mM EDTA, and 1.6 mg/ml Blue Dextran). The samples are then heated to 90°C for three min and loaded into the gel sample wells for sequence analysis by the ABI377 sequencer. Sequence analysis is performed by importing ABI373A files into the Sequencher program (Gene Codes, Ann Arbor, MI). Generally, sequence reads of 700 bp are obtained. Potential sequencing errors are minimized by obtaining sequence information from both DNA strands and by re-sequencing difficult areas using primers at different locations until all sequencing ambiguities are removed.

To isolate a cDNA clone encoding full length nGPCR, a DNA fragment corresponding to a nucleotide sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134, or a portion thereof, can be used as a probe for hybridization screening of a phage cDNA library. The DNA fragment is amplified by the polymerase chain reaction (PCR) method. The PCR reaction mixture of 50μl contains polymerase mixture (0.2mM dNTPs, 1x PCR Buffer and 0.75μl Expand High Fidelity Polymerase (Roche Biochemicals)), 1μg of 3206491 plasmid, and 50pmoles of forward primer and 50pmoles of reverse primer. The primers are preferably 10 to 25 nucleotides in length and are determined by procedures well known to those skilled in the art. Amplification is performed in an Applied Biosystems PE2400 thermocycler, using the following program:

95°C for 15 seconds, 52°C for 30 seconds and 72°C for 90 seconds; repeated for 25 cycles. The amplified product is separated from the plasmid by agarose gel electrophoresis, and purified by Qiaquick gel extraction kit (Qiagen).

A lambda phage library containing cDNAs cloned into lambda ZAPII phage-vector is plated with E. coli XL-1 blue host, on 15 cm LB-agar plates at a density of 50,000 pfu per plate, and grown overnight at 37°C; (plated as described by Sambrook *et al.*, *supra*). Phage plaques are transferred to nylon membranes (Amersham Hybond NJ), denatured for 2 minutes in denaturation solution (0.5 M NaOH, 1.5 M NaCl), renatured for 5 minutes in renaturation solution (1 M Tris pH 7.5, 1.5 M NaCl), and washed briefly in 2xSSC (20x SSC: 3 M NaCl, 0.3 M Na-citrate). Filter membranes are dried and incubated at 80°C for 120 minutes to cross link the phage DNA to the membranes.

The membranes are hybridized with a DNA probe prepared as described above. A DNA fragment (25ng) is labeled with α-^{32}P-dCTP (NEN) using Rediprime random priming (Amersham Pharmacia Biotech), according to the manufacturer's instructions. Labeled DNA is separated from unincorporated nucleotides by S200 spin columns (Amersham Pharmacia Biotech), denatured at 95°C for 5 minutes and kept on ice. The DNA-containing membranes (above) are pre-hybridized in 50ml ExpressHyb (Clontech) solution at 68°C for 90 minutes. Subsequently, the labeled DNA probe is added to the hybridization solution, and the probe is left to hybridize to the membranes at 68°C for 70 minutes. The membranes are washed five times in 2x SSC, 0.1% SDS at 42°C for 5 minutes each, and finally washed 30 minutes in 0.1x SSC, 0.2% SDS. Filters are exposed to Kodak XAR film (Eastman Kodak Company, Rochester, N.Y., USA) with an intensifying screen at –80°C for 16 hours. One positive colony is isolated from the plates, and re-plated with about 1000 pfu on a 15 cm LB plate. Plating, plaque lift to filters and hybridization are performed as described above. About four positive phage plaques are isolated form this secondary screening.

cDNA containing plasmids (pBluescript SK-) are rescued from the isolated phages by in vivo excision by culturing XL-1 blue cells co-infected with the isolated phages and with the Excision helper phage, as described by the manufacturer (Stratagene). XL-blue cells containing the plasmids are plated on LB plates and grown at 37°C for 16 hours. Colonies (18) from each plate are replated on LB plates and grown. One colony from each

plate is stricken onto a nylon filter in an ordered array, and the filter is placed on a LB plate to raise the colonies. The filter is then hybridized with a labeled probe as described above. About three positive colonies are selected and grown up in LB medium. Plasmid DNA is isolated from the three clones by Qiagen Midi Kit (Qiagen) according to the manufacturer's instructions. The size of the insert is determined by digesting the plasmid with the restriction enzymes NotI and SalI, which establishes an insert size. The sequence of the entire insert is determined by automated sequencing on both strands of the plasmids.

EXAMPLE 3: SUBCLONING OF THE CODING REGION OF nGPCR-X VIA PCR

Additional experiments may be conducted to subclone the coding region of nGPCR and place the isolated coding region into a useful vector. Two additional PCR primers are designed based on the coding region of nGPCR, corresponding to either end. To protect against exonucleolytic attack during subsequent exposure to enzymes, *e.g.*, Taq polymerase, primers are routinely synthesized with a protective run of nucleotides at the 5' end that were not necessarily complementary to the desired target.

PCR is performed in a 50μl reaction containing 34μl H_2O, 5 μl 10X TT buffer (140 mM ammonium sulfate, 0.1% gelatin, 0.6 M Tris-tricine, pH 8.4), 5μl 15mM $MgSO_4$, 2μl dNTP mixture (dGTP, dATP, dTTP, and dCTP, each at 10 mM), 3μl genomic phage DNA (0.25μg/μl), 0.3μl Primer 1 (1μg/μl), 0.3μl Primer 2 (1μg/μl), 0.4μl High Fidelity Taq polymerase (Boehringer Mannheim). The PCR reaction was started with 1 cycle of 94°C for 2 minutes; followed by 25 cycles at 94°C for 30 seconds, 55°C for 30 seconds, and 72°C for 1.3 minutes.

The contents from the PCR reaction are loaded onto a 2% agarose gel and fractionated. The DNA band of expected size is excised from the gel, placed in a GenElute Agarose spin column (Supelco) and spun for 10 minutes at maximum speed in a microfuge. The eluted DNA is precipitated with ethanol and resuspended in 6μl H_2O for ligation.

The PCR-amplified DNA fragment containing the coding region is cloned into pCR2.1 using a protocol standard in the art. In particular, the ligation reaction consists of 6μl of GPCR DNA, 1μl 10X ligation buffer, 2μl pCR2.1 (25ng/μl, Invitrogen), and 1μl T4

DNA ligase (Invitrogen). The reaction mixture is incubated overnight at 14°C and the reaction is then stopped by heating at 65°C for 10 minutes. Two microliters of the ligation reaction are transformed into One Shot cells (Invitrogen) and plated onto ampicillin plates. A single colony containing a recombinant pCR2.1 bearing an insert is used to inoculate a 5ml culture of LB medium. Plasmid DNA is purified using the Concert Rapid Plasmid Miniprep System (GibcoBRL) and sequenced. Following confirmation of the sequence, a 50 ml culture of LB medium is inoculated with the transformed One Shot cells, cultured, and processed using a Qiagen Plasmid Midi Kit to yield purifiedpCR-GPCR.

nGPCR-74

PCR was performed in a 50 µl reaction using components that come with PLATINUM® *Pfx* DNA Polymerase (GibcoBRL) containing 30.5 µl H_2O, 5 µl 10X Pfx Amplification buffer, 5 µl 10X Enhancer solution, 1.5 µl 50mM $MgSO_4$, 2 µl 10 mM dNTP, 5 µl human genomic DNA (0.3µg/µl)(Clontech), 0.3 µl of LW1591 (SEQ ID NO: 3)(1 µg/µl), 0.3 µl of LW1592 (SEQ ID NO: 4) (1 µg/µl), 0.4 µl PLATINUM® *Pfx* DNA Polymerase (2.5 U/µl). The PCR reaction was performed in a Robocycler Gradient 96 (Stratagene) starting with 1 cycle of 94°C for 5 min followed by 30 cycles at 94°C for 30 sec, 55°C for 2 min, 68°C for 3 min. Following the final cycle, 0.5 µl of AmpliTaq DNA Polymerase (5 U/µl) was added and the tube was incubated at 72°C for 5 min. The PCR reaction was loaded onto a 1.2% agarose gel. The DNA band was excised from the gel, placed in GenElute Agarose spin column (Supelco) and spun for 10 min at maximum speed in a microcentrifuge. The eluted DNA was EtOH precipitated and resuspended in 121 H_2O for ligation. The forward PCR primer sequence was:

LW1591: GATCAAGCTTGGATGAACCAGACTTTGAATAGC (SEQ ID NO:272) and the reverse PCR primer was:

LW1592: GATCCTCGAGCTCAAGCCCCCATCTCATTGG (SEQ ID NO: 273)

The ligation reaction used solutions from the TOPO TA Cloning Kit (Invitrogen) which consisted of 4µl PCR product DNA and 1 µl pCRII-TOPO vector that was incubated for 5 minutes at room temperature. To the ligation reaction one microliter of 6X TOPO Cloning Stop Solution was added then the reaction was placed on ice. Two microliters of the ligation reaction was transformed in One-Shot TOP10 cells (Invitrogen), and placed on ice

for 30 minutes. The cells were heat-shocked for 30 seconds at 42°C, placed on ice for two minutes, 250 µl of SOC was added, then incubated at 37°C with shaking for one hour and then plated onto ampicillin plates. A single colony containing an insert was used to inoculate a 5 ml culture of LB medium. Plasmid DNA was purified using a Concert Rapid Plasmid Miniprep System (GibcoBRL) and then sequenced.

The DNA subcloned into pCRII-TOPO was sequenced using the ABI PRISM™ 310 Genetic Analyzer (PE Applied Biosystems) which uses advanced capillary electrophoresis technology and the ABI PRISM™ BigDye™ Terminator Cycle Sequencing Ready Reaction Kit. Each cycle-sequencing reaction contained 6 µl of H_20, 8 µl of BigDye Terminator mix, 5 µl mini-prep DNA (0.1 µg/µl), and 1 µl primer (25 ng/µl) and was performed in a Perkin-Elmer 9600 thermocycler with 25 cycles of 96°C for 10 sec, 50°C for 10 sec, and 60°C for 4 min. The product was purified using a Centriflex™ gel filtration cartridge, dried under vacuum, then dissolved in 16 µl of Template Suppression Reagent (PE Applied Biosystems). The samples were heated at 95°C for 5 min then placed in the 310 Genetic Analyzer.

EXAMPLE 4: HYBRIDIZATION ANALYSIS TO DEMONSTRATE nGPCR-X EXPRESSION IN BRAIN

The expression of nGPCR-x in mammals, such as the rat, may be investigated by *in situ* hybridization histochemistry. To investigate expression in the brain, for example, coronal and sagittal rat brain cryosections (20µm thick) are prepared using a Reichert-Jung cryostat. Individual sections are thaw-mounted onto silanized, nuclease-free slides (CEL Associates, Inc., Houston, TX), and stored at -80°C. Sections are processed starting with post-fixation in cold 4% paraformaldehyde, rinsed in cold phosphate-buffered saline (PBS), acetylated using acetic anhydride in triethanolamine buffer, and dehydrated through a series of alcohol washes in 70%, 95%, and 100% alcohol at room temperature. Subsequently, sections are delipidated in chloroform, followed by rehydration through successive exposure to 100% and 95% alcohol at room temperature. Microscope slides containing processed cryosections are allowed to air dry prior to hybridization. Other tissues may be assayed in a similar fashion.

A nGPCR-x-specific probe is generated using PCR. Following PCR amplification, the fragment is digested with restriction enzymes and cloned into pBluescript II cleaved with the same enzymes. For production of a probe specific for the sense strand of nGPCR-x, the nGPCR-x clone in pBluescript II is linearized with a suitable restriction enzyme, which provides a substrate for labeled run-off transcripts (*i.e.*, cRNA riboprobes) using the vector-borne T7 promoter and commercially available T7 RNA polymerase. A probe specific for the antisense strand of nGPCR-x is also readily prepared using the nGPCR-x clone in pBluescript II by cleaving the recombinant plasmid with a suitable restriction enzyme to generate a linearized substrate for the production of labeled run-off cRNA transcripts using the T3 promoter and cognate polymerase. The riboprobes are labeled with [^{35}S]-UTP to yield a specific activity of about 0.40 x 10^6 cpm/pmol for antisense riboprobes and about 0.65 x 10^6 cpm/pmol for sense-strand riboprobes. Each riboprobe is subsequently denatured and added (2 pmol/ml) to hybridization buffer which contained 50% formamide, 10% dextran, 0.3 M NaCl, 10 mM Tris (pH 8.0), 1 mM EDTA, 1X Denhardt's Solution, and 10 mM dithiothreitol. Microscope slides containing sequential brain cryosections are independently exposed to 45μl of hybridization solution per slide and silanized cover slips are placed over the sections being exposed to hybridization solution. Sections are incubated overnight (15-18 hours) at 52°C to allow hybridization to occur. Equivalent series of cryosections are exposed to sense or antisense nGPCR-x-specific cRNA riboprobes.

Following the hybridization period, coverslips are washed off the slides in 1X SSC, followed by RNase A treatment involving the exposure of slides to 20 μg/ml RNase A in a buffer containing 10mM Tris-HCl (pH 7.4), 0.5M EDTA, and 0.5M NaCl for 45 minutes at 37°C. The cryosections are then subjected to three high-stringency washes in 0.1 X SSC at 52°C for 20 minutes each. Following the series of washes, cryosections are dehydrated by consecutive exposure to 70%, 95%, and 100% ammonium acetate in alcohol, followed by air drying and exposure to Kodak BioMax™ MR-1 film. After 13 days of exposure, the film is developed. Based on these results, slides containing tissue that hybridized, as shown by film autoradiograms, are coated with Kodak NTB-2 nuclear track emulsion and the slides are stored in the dark for 32 days. The slides are then developed and counterstained with hematoxylin. Emulsion-coated sections are analyzed

microscopically to determine the specificity of labeling. The signal is determined to be specific if autoradiographic grains (generated by antisense probe hybridization) are clearly associated with cresyl violate-stained cell bodies. Autoradiographic grains found between cell bodies indicates non-specific binding of the probe.

As discussed above, it is well known that GPCRs are expressed in many different tissues and regions, including in the brain. Expression of nGPCR-x in the brain provides an indication that modulators of nGPCR-x activity have utility for treating neurological disorders, including but not limited to, mental disorder, affective disorders, ADHD/ADD (*i.e.*, Attention Deficit-Hyperactivity Disorder/Attention Deficit Disorder), and neural disorders such as Alzheimer's disease, Parkinson's disease, migraine, and senile dementia. Some other diseases for which modulators of nGPCR-x may have utility include depression, anxiety, bipolar disease, epilepsy, neuritis, neurasthenia, neuropathy, neuroses, and the like. Use of nGPCR-x modulators, including nGPCR-x ligands and anti-nGPCR-x antibodies, to treat individuals having such disease states is intended as an aspect of the invention.

EXAMPLE 5: TISSUE EXPRESSION PROFILING

Tissue specific expression of nGPCR-74 was detected using a PCR-based method. Tissue specific expression of cDNAs encoding nGPCR-x may be accomplished using similar methods.

A PCR-based system (RapidScan™ Gene Expression Panel, OriGene Technologies, Rockville, MD) may be used to generate a comprehensive expression profile of the putative nGPCR-x in human tissue, and in human brain regions. The RapidScan Expression Panel is comprised of first-strand cDNAs from various human tissues and brain regions that are serially diluted over a 4-log range and arrayed into a multi-well PCR plate. Human tissues in the array may include: brain, heart, kidney, spleen, liver, colon, lung, small intestine, muscle, stomach, testis, placenta, salivary gland, thyroid, adrenal gland, pancreas, ovary, uterus, prostate, skin, PBL, bone marrow, fetal brain, and fetal liver.

Expression of nGPCR-x in various tissues is detected using PCR primers designed based on the available sequence of the receptor that will prime the synthesis of a predetermined size fragment in the presence of the appropriate cDNA.

PCR is performed in a 50μl reaction containing 34μl H_2O, 5μl 10X TT buffer (140 mM ammonium sulfate, 0.1% gelatin, 0.6 M Tris-tricine, pH 8.4), 5μl 15mM $MgSO_4$, 2μl dNTP mixture (dGTP, dATP, dTTP, and dCTP, each at 10mM), 0.3μl forward primer (1μg/μl), 0.3μl reverse primer (1μg/μl), 0.4μl High Fidelity Taq polymerase (Boehringer Mannheim). The PCR reaction mixture is added to each well of the PCR plate. The plate is placed in a MJ Research PTC100 thermocycler, and is then exposed to the following cycling parameters: Pre-soak 94°C for 3 min; denaturation at 94°C for 30 seconds; annealing at primer 57°C for 45 seconds; extension 72°C for 2 minutes; for 35 cycles. PCR productions are then separated and analyzed by electrophoresis on a 1.2% agarose gel stained with ethidium bromide.

The 4-log dilution range of cDNA deposited on the plate ensures that the amplification reaction is within the linear range and, hence, facilitates semi-quantitative determination of relative mRNA accumulation in the various tissues or brain regions examined.

Primers were synthesized by Genosys Corp., The Woodlands, TX. PCR reactions were assembled using the components of the Expand Hi-Fi PCR System™ (Roche Molecular Biochemicals, Indianapolis, IN).

For nGPCR-74, the above procedure was followed. Multiple Choice™ first strand cDNAs (OriGene Technologies, Rockville, MD) from 12 human tissues were serially diluted over a 3-log range and arrayed into a multi-well PCR plate. This array was used to generate a comprehensive expression profile of the putative GPCR in human tissues. Human tissues arrayed include: brain, heart, kidney, peripheral blood leukocytes, liver, lung, muscle, ovary, prostate, small intestine, spleen and testis. The forward primer used was:

5'CTGTCTCTCTGTCCTCTTCC (SEQ ID NO: 270),

and the reverse primer used was:

5'GCACCGATCTTCATTGAATTTC (SEQ ID NO: 271). This primer set primed the synthesis of a 157 base pair fragment in the presence of the appropriate cDNA. For

detection of expression within brain regions, the same primer set was used with the Human Brain Rapid Scan™ Panel (OriGene Technologies, Rockville, MD). This panel represents serial dilutions over a 2 log range of first strand cDNA from the following brain regions arrayed in a 96 well format: frontal lobe, temporal lobe, cerebellum, hippocampus, substantia nigra, caudate nucleus, amygdala, thalamus, hypothalamus, pons, medulla and spinal cord. Primers were synthesized by Genosys Corp., The Woodlands, TX. PCR reactions were assembled using the components of the Expand Hi-Fi PCR System™ (Roche Molecular Biochemicals, Indianapolis, IN). Twenty-five microliters of the PCR reaction mixture was added to each well of the RapidScan PCR plate. The plate was placed in a GeneAmp 9700 PCR thermocycler (Perkin Elmer Applied Biosystems). The following cycling program was executed: Pre-soak at (94° for 3min.) followed by 35 cycles of [(94° for 45 sec.) (53°C for 2 min.) (72° for 45 sec)]. PCR reaction products were then separated and analyzed by electrophoresis on a 2.0% agarose gel stained with ethidium bromide.

nGPCR-74 was expressed in the brain, heart, kidney, peripheral blood leukocytes, liver, lung, muscle, ovary, prostate, small intestine, spleen, and testis. Within the brain, nGPCR-74 was expressed in the frontal and temporal lobes, cerebellum, hippocampus, substantia nigra, amygdala, thalamus, pons, and spinal cord.

Expression of the nGPCR-74 in the brain provides an indication that modulators of nGPCR-74 activity have utility for treating neurological disorders, including but not limited to, schizophrenia, affective disorders, ADHD/ADD (*i.e.*, Attention Deficit-Hyperactivity Disorder/Attention Deficit Disorder), neural disorders such as Alzheimer's disease, Parkinson's disease, migraine, senile dementia, depression, anxiety, bipolar disease, epilepsy, neuritis, neurasthenia, neuropathy, neuroses, metabolic disorders, inflammatory disorders, cancers and the like. Use of nGPCR-74 modulators, including nGPCR-74 ligands and anti-nGPCR-74 antibodies, to treat individuals having such disease states is intended as an aspect of the invention.

EXAMPLE 6: NORTHERN BLOT ANALYSIS

Northern blots are performed to examine the expression of nGPCR-x mRNA. The sense orientation oligonucleotide and the antisense-orientation oligonucleotide, described

above, are used as primers to amplify a portion of the GPCR-x cDNA sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134.

Multiple human tissue northern blots from Clontech (Human II # 7767-1) are hybridized with the probe. Pre-hybridization is carried out at 42 C for 4 hours in 5xSSC, 1X Denhardt's reagent, 0.1% SDS, 50% formamide, 250 mg/ml salmon sperm DNA. Hybridization is performed overnight at 42°C in the same mixture with the addition of about $1.5x10^6$ cpm/ml of labeled probe.

The probe is labeled with α-^{32}P-dCTP by Rediprime™ DNA labeling system (Amersham Pharmacia), purified on Nick Column™ (Amersham Pharmacia) and added to the hybridization solution. The filters are washed several times at 42°C in 0.2x SSC, 0.1% SDS. Filters are exposed to Kodak XAR film (Eastman Kodak Company, Rochester, N.Y., USA) with intensifying screen at –80°C.

EXAMPLE 7: RECOMBINANT EXPRESSION OF nGPCR-X IN EUKARYOTIC HOST CELLS

A. Expression of nGPCR-x in Mammalian Cells

To produce nGPCR-x protein, a nGPCR-x-encoding polynucleotide is expressed in a suitable host cell using a suitable expression vector and standard genetic engineering techniques. For example, the nGPCR-x-encoding sequence described in Example 1 is subcloned into the commercial expression vector pzeoSV2 (Invitrogen, San Diego, CA) and transfected into Chinese Hamster Ovary (CHO) cells using the transfection reagent FuGENE6™ (Boehringer-Mannheim) and the transfection protocol provided in the product insert. Other eukaryotic cell lines, including human embryonic kidney (HEK 293) and COS cells, are suitable as well. Cells stably expressing nGPCR-x are selected by growth in the presence of 100µg/ml zeocin (Stratagene, LaJolla, CA). Optionally, nGPCR-x may be purified from the cells using standard chromatographic techniques. To facilitate purification, antisera is raised against one or more synthetic peptide sequences that correspond to portions of the nGPCR-x amino acid sequence, and the antisera is used to affinity purify nGPCR-x. The nGPCR-x also may be expressed in-frame with a tag sequence (*e.g.*, polyhistidine, hemagluttinin, FLAG) to facilitate purification. Moreover, it

will be appreciated that many of the uses for nGPCR-x polypeptides, such as assays described below, do not require purification of nGPCR-x from the host cell.

B. Expression of nGPCR-x in HEK-293 cells

For expression of nGPCR-x in mammalian cells HEK293 (transformed human, primary embryonic kidney cells), a plasmid bearing the relevant nGPCR-x coding sequence is prepared, using vector pSecTag2A (Invitrogen). Vector pSecTag2A contains the murine IgK chain leader sequence for secretion, the c-myc epitope for detection of the recombinant protein with the anti-myc antibody, a C-terminal polyhistidine for purification with nickel chelate chromatography, and a Zeocin resistant gene for selection of stable transfectants. The forward primer for amplification of this GPCR cDNA is determined by routine procedures and preferably contains a 5' extension of nucleotides to introduce the *HindIII* cloning site and nucleotides matching the GPCR sequence. The reverse primer is also determined by routine procedures and preferably contains a 5' extension of nucleotides to introduce an *XhoI* restriction site for cloning and nucleotides corresponding to the reverse complement of the nGPCR-x sequence. The PCR conditions are 55°C as the annealing temperature. The PCR product is gel purified and cloned into the *HindIII-XhoI* sites of the vector.

The DNA is purified using Qiagen chromatography columns and transfected into HEK-293 cells using DOTAP™ transfection media (Boehringer Mannheim, Indianapolis, IN). Transiently transfected cells are tested for expression after 24 hours of transfection, using western blots probed with anti-His and anti-nGPCR-x peptide antibodies. Permanently transfected cells are selected with Zeocin and propagated. Production of the recombinant protein is detected from both cells and media by western blots probed with anti-His, anti-Myc or anti-GPCR peptide antibodies.

C. Expression of nGPCR-x in COS cells

For expression of the nGPCR-x in COS7 cells, a polynucleotide molecule having a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134 can be cloned into vector p3-CI. This vector is a pUC18-derived plasmid that contains the HCMV (human cytomegalovirus) promoter-intron located upstream from the bGH (bovine growth hormone) polyadenylation sequence and a multiple cloning site. In addition, the

plasmid contains the dhrf (dihydrofolate reductase) gene which provides selection in the presence of the drug methotrexane (MTX) for selection of stable transformants.

The forward primer is determined by routine procedures and preferably contains a 5' extension which introduces an *XbaI* restriction site for cloning, followed by nucleotides which correspond to a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134. The reverse primer is also determined by routine procedures and preferably contains 5'- extension of nucleotides which introduces a *SalI* cloning site followed by nucleotides which correspond to the reverse complement of a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134. The PCR consists of an initial denaturation step of 5 min at 95°C 30 cycles of 30 sec denaturation at 95°C, 30 sec annealing at 58°C and 30 sec extension at 72°C, followed by 5 min extension at 72°C. The PCR product is gel purified and ligated into the *XbaI* and *SalI* sites of vector p3-CI. This construct is transformed into *E. coli* cells for amplification and DNA purification. The DNA is purified with Qiagen chromatography columns and transfected into COS 7 cells using Lipofectamine™ reagent from BRL, following the manufacturer's protocols. Forty-eight and 72 hours after transfection, the media and the cells are tested for recombinant protein expression.

nGPCR-x expressed from a COS cell culture can be purified by concentrating the cell-growth media to about 10 mg of protein/ml, and purifying the protein by, for example, chromatography. Purified nGPCR-x is concentrated to 0.5 mg/ml in an Amicon concentrator fitted with a YM-10 membrane and stored at -80°C.

D. Expression of nGPCR-x in Insect Cells

For expression of nGPCR-x in a baculovirus system, a polynucleotide molecule having a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134 can be amplified by PCR. The forward primer is determined by routine procedures and preferably contains a 5' extension which adds the *NdeI* cloning site, followed by nucleotides which correspond to a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134. The reverse primer is also determined by routine procedures and preferably contains a 5' extension which introduces the *KpnI* cloning site, followed by

nucleotides which correspond to the reverse complement of a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134.

The PCR product is gel purified, digested with *NdeI* and *KpnI*, and cloned into the corresponding sites of vector pACHTL-A (Pharmingen, San Diego, CA). The pAcHTL expression vector contains the strong polyhedrin promoter of the *Autographa californica* nuclear polyhedrosis virus (AcMNPV), and a 6XHis tag upstream from the multiple cloning site. A protein kinase site for phosphorylation and a thrombin site for excision of the recombinant protein precede the multiple cloning site is also present. Of course, many other baculovirus vectors could be used in place of pAcHTL-A, such as pAc373, pVL941 and pAcIM1. Other suitable vectors for the expression of GPCR polypeptides can be used, provided that the vector construct includes appropriately located signals for transcription, translation, and trafficking, such as an in-frame AUG and a signal peptide, as required. Such vectors are described in Luckow *et al.*, Virology 170:31-39, among others.

The virus is grown and isolated using standard baculovirus expression methods, such as those described in Summers *et al.* (A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures, Texas Agricultural Experimental Station Bulletin No. 1555 (1987)).

In a preferred embodiment, pAcHLT-A containing nGPCR-x gene is introduced into baculovirus using the "BaculoGold™" transfection kit (Pharmingen, San Diego, CA) using methods established by the manufacturer. Individual virus isolates are analyzed for protein production by radiolabeling infected cells with ^{35}S-methionine at 24 hours post infection. Infected cells are harvested at 48 hours post infection, and the labeled proteins are visualized by SDS-PAGE. Viruses exhibiting high expression levels can be isolated and used for scaled up expression.

For expression of a nGPCR-x polypeptide in a Sf9 cells, a polynucleotide molecule having a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134 can be amplified by PCR using the primers and methods described above for baculovirus expression. The nGPCR-x cDNA is cloned into vector pAcHLT-A (Pharmingen) for expression in Sf9 insect. The insert is cloned into the *NdeI* and *KpnI* sites, after elimination of an internal *NdeI* site (using the same primers described above for

expression in baculovirus). DNA is purified with Qiagen chromatography columns and expressed in Sf9 cells. Preliminary Western blot experiments from non-purified plaques are tested for the presence of the recombinant protein of the expected size which reacted with the GPCR-specific antibody. These results are confirmed after further purification and expression optimization in HiG5 cells.

EXAMPLE 8: INTERACTION TRAP/TWO-HYBRID SYSTEM

In order to assay for nGPCR-x-interacting proteins, the interaction trap/two-hybrid library screening method can be used. This assay was first described in Fields *et al.*, *Nature,* **1989**, *340*, 245, which is incorporated herein by reference in its entirety. A protocol is published in Current Protocols in Molecular Biology 1999, John Wiley & Sons, NY, and Ausubel, F. M. *et al.* 1992, Short protocols in molecular biology, Fourth edition, Greene and Wiley-interscience, NY, each of which is incorporated herein by reference in its entirety. Kits are available from Clontech, Palo Alto, CA (Matchmaker Two-Hybrid System 3).

A fusion of the nucleotide sequences encoding all or partial nGPCR-x and the yeast transcription factor GAL4 DNA-binding domain (DNA-BD) is constructed in an appropriate plasmid (*i.e.*, pGBKT7) using standard subcloning techniques. Similarly, a GAL4 active domain (AD) fusion library is constructed in a second plasmid (*i.e.*, pGADT7) from cDNA of potential GPCR-binding proteins (for protocols on forming cDNA libraries, see Sambrook *et al.* 1989, Molecular cloning: a laboratory manual, second edition, Cold Spring Harbor Press, Cold Spring Harbor, NY), which is incorporated herein by reference in its entirety. The DNA-BD/nGPCR-x fusion construct is verified by sequencing, and tested for autonomous reporter gene activation and cell toxicity, both of which would prevent a successful two-hybrid analysis. Similar controls are performed with the AD/library fusion construct to ensure expression in host cells and lack of transcriptional activity. Yeast cells are transformed (*ca.* 105 transformants/mg DNA) with both the nGPCR-x and library fusion plasmids according to standard procedures (Ausubel *et al.*, 1992, Short protocols in molecular biology, fourth edition, Greene and Wiley-interscience, NY, which is incorporated herein by reference in its entirety). *In vivo* binding of DNA-BD/nGPCR-x with AD/library proteins results in

transcription of specific yeast plasmid reporter genes (*i.e.*, lacZ, HIS3, ADE2, LEU2). Yeast cells are plated on nutrient-deficient media to screen for expression of reporter genes. Colonies are dually assayed for β-galactosidase activity upon growth in Xgal (5-bromo-4-chloro-3-indolyl-β-D-galactoside) supplemented media (filter assay for β-galactosidase activity is described in Breeden *et al.,* Cold Spring Harb. Symp. Quant. Biol., 1985, 50, 643, which is incorporated herein by reference in its entirety). Positive AD-library plasmids are rescued from transformants and reintroduced into the original yeast strain as well as other strains containing unrelated DNA-BD fusion proteins to confirm specific nGPCR-x/library protein interactions. Insert DNA is sequenced to verify the presence of an open reading frame fused to GAL4 AD and to determine the identity of the nGPCR-x-binding protein.

EXAMPLE 9: MOBILITY SHIFT DNA-BINDING ASSAY USING GEL ELECTROPHORESIS

A gel electrophoresis mobility shift assay can rapidly detect specific protein-DNA interactions. Protocols are widely available in such manuals as Sambrook *et al.* **1989**, *Molecular cloning: a laboratory* manual, second edition, Cold Spring Harbor Press, Cold Spring Harbor, NY and Ausubel, F. M. *et al.*, 1992, Short Protocols in Molecular Biology, fourth edition, Greene and Wiley-interscience, NY, each of which is incorporated herein by reference in its entirety.

Probe DNA(<300 bp) is obtained from synthetic oligonucleotides, restriction endonuclease fragments, or PCR fragments and end-labeled with ^{32}P. An aliquot of purified nGPCR-x (*ca.* 15 μg) or crude nGPCR-x extract (*ca.* 15 ng) is incubated at constant temperature (in the range 22-37 C) for at least 30 minutes in 10-15 μl of buffer (*i.e.* TAE or TBE, pH 8.0-8.5) containing radiolabeled probe DNA, nonspecific carrier DNA (*ca.* 1 μg), BSA (300 μg/ml), and 10% (v/v) glycerol. The reaction mixture is then loaded onto a polyacrylamide gel and run at 30-35 mA until good separation of free probe DNA from protein-DNA complexes occurs. The gel is then dried and bands corresponding to free DNA and protein-DNA complexes are detected by autoradiography.

EXAMPLE 10: ANTIBODIES TO nGPCR-X

Standard techniques are employed to generate polyclonal or monoclonal antibodies to the nGPCR-x receptor, and to generate useful antigen-binding fragments thereof or variants thereof, including "humanized" variants. Such protocols can be found, for example, in Sambrook *et al.* (1989) and Harlow *et al.* (Eds.), Antibodies A Laboratory Manual; Cold Spring Harbor Laboratory; Cold Spring Harbor, NY (1988). In one embodiment, recombinant nGPCR-x polypeptides (or cells or cell membranes containing such polypeptides) are used as antigen to generate the antibodies. In another embodiment, one or more peptides having amino acid sequences corresponding to an immunogenic portion of nGPCR-x (*e.g.*, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20,or more amino acids) are used as antigen. Peptides corresponding to extracellular portions of nGPCR-x, especially hydrophilic extracellular portions, are preferred. The antigen may be mixed with an adjuvant or linked to a hapten to increase antibody production.

A. Polyclonal or Monoclonal antibodies

As one exemplary protocol, recombinant nGPCR-x or a synthetic fragment thereof is used to immunize a mouse for generation of monoclonal antibodies (or larger mammal, such as a rabbit, for polyclonal antibodies). To increase antigenicity, peptides are conjugated to Keyhole Lympet Hemocyanin (Pierce), according to the manufacturer's recommendations. For an initial injection, the antigen is emulsified with Freund's Complete Adjuvant and injected subcutaneously. At intervals of two to three weeks, additional aliquots of nGPCR-x antigen are emulsified with Freund's Incomplete Adjuvant and injected subcutaneously. Prior to the final booster injection, a serum sample is taken from the immunized mice and assayed by western blot to confirm the presence of antibodies that immunoreact with nGPCR-x. Serum from the immunized animals may be used as polyclonal antisera or used to isolate polyclonal antibodies that recognize nGPCR-x. Alternatively, the mice are sacrificed and their spleen removed for generation of monoclonal antibodies.

To generate monoclonal antibodies, the spleens are placed in 10 ml serum-free RPMI 1640, and single cell suspensions are formed by grinding the spleens in serum-free RPMI 1640, supplemented with 2 mM L-glutamine, 1 mM sodium pyruvate, 100 units/ml penicillin, and 100 μg/ml streptomycin (RPMI) (Gibco, Canada). The cell suspensions are

filtered and washed by centrifugation and resuspended in serum-free RPMI. Thymocytes taken from three naive Balb/c mice are prepared in a similar manner and used as a Feeder Layer. NS-1 myeloma cells, kept in log phase in RPMI with 10% fetal bovine serum (FBS) (Hyclone Laboratories, Inc., Logan, Utah) for three days prior to fusion, are centrifuged and washed as well.

To produce hybridoma fusions, spleen cells from the immunized mice are combined with NS-1 cells and centrifuged, and the supernatant is aspirated. The cell pellet is dislodged by tapping the tube, and 2 ml of 37°C PEG 1500 (50% in 75 mM HEPES, pH 8.0) (Boehringer-Mannheim) is stirred into the pellet, followed by the addition of serum-free RPMI. Thereafter, the cells are centrifuged, resuspended in RPMI containing 15% FBS, 100 µM sodium hypoxanthine, 0.4 µM aminopterin, 16 µM thymidine (HAT) (Gibco), 25 units/ml IL-6 (Boehringer-Mannheim) and 1.5 x 10^6 thymocytes/ml, and plated into 10 Corning flat-bottom 96-well tissue culture plates (Corning, Corning New York).

On days 2, 4, and 6 after the fusion, 100µl of medium is removed from the wells of the fusion plates and replaced with fresh medium. On day 8, the fusions are screened by ELISA, testing for the presence of mouse IgG that binds to nGPCR-x. Selected fusion wells are further cloned by dilution until monoclonal cultures producing anti-nGPCR-x antibodies are obtained.

B. <u>Humanization of anti-nGPCR-x monoclonal antibodies</u>

The expression pattern of nGPCR-x as reported herein and the proven track record of GPCRs as targets for therapeutic intervention suggest therapeutic indications for nGPCR-x inhibitors (antagonists). nGPCR-x-neutralizing antibodies comprise one class of therapeutics useful as nGPCR-x antagonists. Following are protocols to improve the utility of anti-nGPCR-x monoclonal antibodies as therapeutics in humans by "humanizing" the monoclonal antibodies to improve their serum half-life and render them less immunogenic in human hosts (*i.e.*, to prevent human antibody response to non-human anti-nGPCR-x antibodies).

The principles of humanization have been described in the literature and are facilitated by the modular arrangement of antibody proteins. To minimize the possibility of binding complement, a humanized antibody of the IgG4 isotype is preferred.

For example, a level of humanization is achieved by generating chimeric antibodies comprising the variable domains of non-human antibody proteins of interest with the constant domains of human antibody molecules. (See, *e.g.*, Morrison *et al.*, Adv. Immunol., 44:65-92 (1989)). The variable domains of nGPCR-x-neutralizing anti-nGPCR-x antibodies are cloned from the genomic DNA of a B-cell hybridoma or from cDNA generated from mRNA isolated from the hybridoma of interest. The V region gene fragments are linked to exons encoding human antibody constant domains, and the resultant construct is expressed in suitable mammalian host cells (*e.g*, myeloma or CHO cells).

To achieve an even greater level of humanization, only those portions of the variable region gene fragments that encode antigen-binding complementarity determining regions ("CDR") of the non-human monoclonal antibody genes are cloned into human antibody sequences. (See, *e.g.*, Jones *et al.*, Nature 321:522-525 (1986); Riechmann *et al.*, Nature 332:323-327 (1988); Verhoeyen *et al.*, Science 239:1534-36 (1988); and Tempest *et al.*, Bio/Technology 9: 266-71 (1991)). If necessary, the β-sheet framework of the human antibody surrounding the CDR3 regions also is modified to more closely mirror the three dimensional structure of the antigen-binding domain of the original monoclonal antibody. (See Kettleborough *et al.*, Protein Engin., 4:773-783 (1991); and Foote *et al.*, J. Mol. Biol., 224:487-499 (1992)).

In an alternative approach, the surface of a non-human monoclonal antibody of interest is humanized by altering selected surface residues of the non-human antibody, *e.g.*, by site-directed mutagenesis, while retaining all of the interior and contacting residues of the non-human antibody. See Padlan, Molecular Immunol., 28(4/5):489-98 (1991).

The foregoing approaches are employed using nGPCR-x-neutralizing anti-nGPCR-x monoclonal antibodies and the hybridomas that produce them to generate humanized nGPCR-x-neutralizing antibodies useful as therapeutics to treat or palliate conditions wherein nGPCR-x expression or ligand-mediated nGPCR-x signaling is detrimental.

C. Human nGPCR-x-Neutralizing Antibodies from Phage Display

Human nGPCR-x-neutralizing antibodies are generated by phage display techniques such as those described in Aujame *et al.*, Human Antibodies 8(4):155-168

(1997); Hoogenboom, TIBTECH 15:62-70 (1997); and Rader *et al.*, Curr. Opin. Biotechnol. 8:503-508 (1997), all of which are incorporated by reference. For example, antibody variable regions in the form of Fab fragments or linked single chain Fv fragments are fused to the amino terminus of filamentous phage minor coat protein pIII. Expression of the fusion protein and incorporation thereof into the mature phage coat results in phage particles that present an antibody on their surface and contain the genetic material encoding the antibody. A phage library comprising such constructs is expressed in bacteria, and the library is screened for nGPCR-x-specific phage-antibodies using labeled or immobilized nGPCR-x as antigen-probe.

D. Human nGPCR-x-neutralizing antibodies from transgenic mice

Human nGPCR-x-neutralizing antibodies are generated in transgenic mice essentially as described in Bruggemann *et al.*, Immunol. Today 17(8):391-97 (1996) and Bruggemann *et al.*, Curr. Opin. Biotechnol. 8:455-58 (1997). Transgenic mice carrying human V-gene segments in germline configuration and that express these transgenes in their lymphoid tissue are immunized with a nGPCR-x composition using conventional immunization protocols. Hybridomas are generated using B cells from the immunized mice using conventional protocols and screened to identify hybridomas secreting anti-nGPCR-x human antibodies (*e.g.*, as described above).

EXAMPLE 11: ASSAYS TO IDENTIFY MODULATORS OF nGPCR-X ACTIVITY

Set forth below are several nonlimiting assays for identifying modulators (agonists and antagonists) of nGPCR-x activity. Among the modulators that can be identified by these assays are natural ligand compounds of the receptor; synthetic analogs and derivatives of natural ligands; antibodies, antibody fragments, and/or antibody-like compounds derived from natural antibodies or from antibody-like combinatorial libraries; and/or synthetic compounds identified by high-throughput screening of libraries; and the like. All modulators that bind nGPCR-x are useful for identifying nGPCR-x in tissue samples (*e.g.*, for diagnostic purposes, pathological purposes, and the like). Agonist and antagonist modulators are useful for up-regulating and down-regulating nGPCR-x activity, respectively, to treat disease states characterized by abnormal levels of nGPCR-x activity.

The assays may be performed using single putative modulators, and/or may be performed using a known agonist in combination with candidate antagonists (or visa versa).

A. cAMP Assays

In one type of assay, levels of cyclic adenosine monophosphate (cAMP) are measured in nGPCR-x-transfected cells that have been exposed to candidate modulator compounds. Protocols for cAMP assays have been described in the literature. (See,*e.g.*, Sutherland *et al.*, Circulation 37: 279 (1968); Frandsen *et al.*, Life Sciences 18: 529-541 (1976); Dooley *et al.*, Journal of Pharmacology and Experimental Therapeutics 283 (2): 735-41 (1997); and George *et al.*, Journal of Biomolecular Screening 2 (4): 235-40 (1997)). An exemplary protocol for such an assay, using an Adenylyl Cyclase Activation FlashPlate® Assay from NEN™ Life Science Products, is set forth below.

Briefly, the nGPCR-x coding sequence (*e.g.*, a cDNA or intronless genomic DNA) is subcloned into a commercial expression vector, such as pzeoSV2 (Invitrogen), and transiently transfected into Chinese Hamster Ovary (CHO) cells using known methods, such as the transfection protocol provided by Boehringer-Mannheim when supplying the FuGENE 6 transfection reagent. Transfected CHO cells are seeded into 96-well microplates from the FlashPlate® assay kit, which are coated with solid scintillant to which antisera to cAMP has been bound. For a control, some wells are seeded with wild type (untransfected) CHO cells. Other wells in the plate receive various amounts of a cAMP standard solution for use in creating a standard curve.

One or more test compounds (*i.e.*, candidate modulators) are added to the cells in each well, with water and/or compound-free medium/diluent serving as a control or controls. After treatment, cAMP is allowed to accumulate in the cells for exactly 15 minutes at room temperature. The assay is terminated by the addition of lysis buffer containing [^{125}I]-labeled cAMP, and the plate is counted using a Packard Topcount™ 96-well microplate scintillation counter. Unlabeled cAMP from the lysed cells (or from standards) and fixed amounts of [^{125}I]-cAMP compete for antibody bound to the plate. A standard curve is constructed, and cAMP values for the unknowns are obtained by interpolation. Changes in intracellular cAMP levels of cells in response to exposure to a test compound are indicative of nGPCR-x modulating activity. Modulators that act as agonists of receptors which couple to the G_s subtype of G proteins will stimulate

production of cAMP, leading to a measurable 3-10 fold increase in cAMP levels. Agonists of receptors which couple to the $G_{i/o}$ subtype of G proteins will inhibit forskolin-stimulated cAMP production, leading to a measurable decrease in cAMP levels of 50-100%. Modulators that act as inverse agonists will reverse these effects at receptors that are either constitutively active or activated by known agonists.

B. Aequorin Assays

In another assay, cells (*e.g.*, CHO cells) are transiently co-transfected with both a nGPCR-x expression construct and a construct that encodes the photoprotein apoaquorin. In the presence of the cofactor coelenterazine, apoaquorin will emit a measurable luminescence that is proportional to the amount of intracellular (cytoplasmic) free calcium. (See generally, Cobbold, *et al.* "Aequorin measurements of cytoplasmic free calcium," *In*: McCormack J.G. and Cobbold P.H., eds., *Cellular Calcium: A Practical Approach*. Oxford:IRL Press (1991); Stables *et al.*, Analytical Biochemistry 252: 115-26 (1997); and Haugland, Handbook of Fluorescent Probes and Research Chemicals. Sixth edition. Eugene OR: Molecular Probes (1996).)

In one exemplary assay, nGPCR-x is subcloned into the commercial expression vector pzeoSV2 (Invitrogen) and transiently co-transfected along with a construct that encodes the photoprotein apoaquorin (Molecular Probes, Eugene, OR) into CHO cells using the transfection reagent FuGENE 6 (Boehringer-Mannheim) and the transfection protocol provided in the product insert.

The cells are cultured for 24 hours at 37°C in MEM (Gibco/BRL, Gaithersburg, MD) supplemented with 10% fetal bovine serum, 2 mM glutamine, 10 U/ml penicillin and 10 µg/ml streptomycin, at which time the medium is changed to serum-free MEM containing 5 µM coelenterazine (Molecular Probes, Eugene, OR). Culturing is then continued for two additional hours at 37°C. Subsequently, cells are detached from the plate using VERSEN (Gibco/BRL), washed, and resuspended at 200,000 cells/ml in serum-free MEM.

Dilutions of candidate nGPCR-x modulator compounds are prepared in serum-free MEM and dispensed into wells of an opaque 96-well assay plate at 50 µl/well. Plates are then loaded onto an MLX microtiter plate luminometer (Dynex Technologies, Inc., Chantilly, VA). The instrument is programmed to dispense 50µl cell suspensions into

each well, one well at a time, and immediately read luminescence for 15 seconds. Dose-response curves for the candidate modulators are constructed using the area under the curve for each light signal peak. Data are analyzed with SlideWrite, using the equation for a one-site ligand, and EC_{50} values are obtained. Changes in luminescence caused by the compounds are considered indicative of modulatory activity. Modulators that act as agonists at receptors which couple to the G_q subtype of G proteins give an increase in luminescence of up to 100 fold. Modulators that act as inverse agonists will reverse this effect at receptors that are either constitutively active or activated by known agonists.

C. Luciferase Reporter Gene Assay

The photoprotein luciferase provides another useful tool for assaying for modulators of nGPCR-x activity. Cells (*e.g.*, CHO cells or COS 7 cells) are transiently co-transfected with both a nGPCR-x expression construct (*e.g.*, nGPCR-x in pzeoSV2) and a reporter construct which includes a gene for the luciferase protein downstream from a transcription factor binding site, such as the cAMP-response element (CRE), AP-1, or NF-kappa B. Agonist binding to receptors coupled to the G_s subtype of G proteins leads to increases in cAMP, thereby activating the CRE transcription factor and resulting in expression of the luciferase gene. Agonist binding to receptors coupled to the G_q subtype of G protein leads to production of diacylglycerol that activates protein kinase C, which activates the AP-1 or NF-kappa B transcription factors, in turn resulting in expression of the luciferase gene. Expression levels of luciferase reflect the activation status of the signaling events. (See generally, George *et al.*, Journal of Biomolecular Screening 2(4): 235-240 (1997); and Stratowa *et al.*, Current Opinion in Biotechnology 6: 574-581 (1995)). Luciferase activity may be quantitatively measured using, *e.g.*, luciferase assay reagents that are commercially available from Promega (Madison, WI).

In one exemplary assay, CHO cells are plated in 24-well culture dishes at a density of 100,000 cells/well one day prior to transfection and cultured at 37°C in MEM (Gibco/BRL) supplemented with 10% fetal bovine serum, 2 mM glutamine, 10 U/ml penicillin and 10 μg/ml streptomycin. Cells are transiently co-transfected with both a nGPCR-x expression construct and a reporter construct containing the luciferase gene. The reporter plasmids CRE-luciferase, AP-1-luciferase and NF-kappaB-luciferase may be purchased from Stratagene (LaJolla, CA). Transfections are performed using the FuGENE

6 transfection reagent (Boehringer-Mannheim) according to the supplier's instructions. Cells transfected with the reporter construct alone are used as a control. Twenty-four hours after transfection, cells are washed once with PBS pre-warmed to 37°C. Serum-free MEM is then added to the cells either alone (control) or with one or more candidate modulators and the cells are incubated at 37°C for five hours. Thereafter, cells are washed once with ice-cold PBS and lysed by the addition of 100 µl of lysis buffer per well from the luciferase assay kit supplied by Promega. After incubation for 15 minutes at room temperature, 15 µl of the lysate is mixed with 50 µl of substrate solution (Promega) in an opaque-white, 96-well plate, and the luminescence is read immediately on a Wallace model 1450 MicroBeta scintillation and luminescence counter (Wallace Instruments, Gaithersburg, MD).

Differences in luminescence in the presence versus the absence of a candidate modulator compound are indicative of modulatory activity. Receptors that are either constitutively active or activated by agonists typically give a 3 to 20-fold stimulation of luminescence compared to cells transfected with the reporter gene alone. Modulators that act as inverse agonists will reverse this effect.

D. <u>Intracellular calcium measurement using FLIPR</u>

Changes in intracellular calcium levels are another recognized indicator of G protein-coupled receptor activity, and such assays can be employed to screen for modulators of nGPCR-x activity. For example, CHO cells stably transfected with a nGPCR-x expression vector are plated at a density of 4 x 10^4 cells/well in Packard black-walled, 96-well plates specially designed to discriminate fluorescence signals emanating from the various wells on the plate. The cells are incubated for 60 minutes at 37°C in modified Dulbecco's PBS (D-PBS) containing 36 mg/L pyruvate and 1 g/L glucose with the addition of 1% fetal bovine serum and one of four calcium indicator dyes (Fluo-3™ AM, Fluo-4™ AM, Calcium Green™-1 AM, or Oregon Green™ 488 BAPTA-1 AM), each at a concentration of 4 µM. Plates are washed once with modified D-PBS without 1% fetal bovine serum and incubated for 10 minutes at 37°C to remove residual dye from the cellular membrane. In addition, a series of washes with modified D-PBS without 1% fetal bovine serum is performed immediately prior to activation of the calcium response.

A calcium response is initiated by the addition of one or more candidate receptor agonist compounds, calcium ionophore A23187 (10 μM; positive control), or ATP (4 μM; positive control). Fluorescence is measured by Molecular Device's FLIPR with an argon laser (excitation at 488 nm). (See, *e.g.*, Kuntzweiler *et al.*, Drug Development Research, 44(1):14-20 (1998)). The F-stop for the detector camera was set at 2.5 and the length of exposure was 0.4 milliseconds. Basal fluorescence of cells was measured for 20 seconds prior to addition of candidate agonist, ATP, or A23187, and the basal fluorescence level was subtracted from the response signal. The calcium signal is measured for approximately 200 seconds, taking readings every two seconds. Calcium ionophore A23187 and ATP increase the calcium signal 200% above baseline levels. In general, activated GPCRs increase the calcium signal approximately 10-15% above baseline signal.

E. Mitogenesis Assay

In a mitogenesis assay, the ability of candidate modulators to induce or inhibit nGPCR-x-mediated cell division is determined. (*See, e.g.*, Lajiness *et al.*, Journal of Pharmacology and Experimental Therapeutics 267(3): 1573-1581 (1993)). For example, CHO cells stably expressing nGPCR-x are seeded into 96-well plates at a density of 5000 cells/well and grown at 37°C in MEM with 10% fetal calf serum for 48 hours, at which time the cells are rinsed twice with serum-free MEM. After rinsing, 80μl of fresh MEM, or MEM containing a known mitogen, is added along with 20μl MEM containing varying concentrations of one or more candidate modulators or test compounds diluted in serum-free medium. As controls, some wells on each plate receive serum-free medium alone, and some receive medium containing 10% fetal bovine serum. Untransfected cells or cells transfected with vector alone also may serve as controls.

After culture for 16-18 hours, 1μ Ci of [^{3}H]-thymidine (2 Ci/mmol) is added to the wells and cells are incubated for an additional 2 hours at 37°C. The cells are trypsinized and collected on filter mats with a cell harvester (Tomtec); the filters are then counted in a Betaplate counter. The incorporation of [^{3}H]-thymidine in serum-free test wells is compared to the results achieved in cells stimulated with serum (positive control). Use of multiple concentrations of test compounds permits creation and analysis of dose-response curves using the non-linear, least squares fit equation: $A = B \times [C/(D + C)] + G$ where A is the percent of serum stimulation; B is the maximal effect minus baseline; C is the EC_{50};

D is the concentration of the compound; and G is the maximal effect. Parameters B,C and G are determined by Simplex optimization.

Agonists that bind to the receptor are expected to increase [^{3}H]-thymidine incorporation into cells, showing up to 80% of the response to serum. Antagonists that bind to the receptor will inhibit the stimulation seen with a known agonist by up to 100%.

F. [^{35}S]GTPγS Binding Assay

Because G protein-coupled receptors signal through intracellular G proteins whose activity involves GTP binding and hydrolysis to yield bound GDP, measurement of binding of the non-hydrolyzable GTP analog [^{35}S]GTPγS in the presence and absence of candidate modulators provides another assay for modulator activity. (*See, e.g*, Kowal *et al.*, Neuropharmacology 37:179-187 (1998).)

In one exemplary assay, cells stably transfected with a nGPCR-x expression vector are grown in 10 cm tissue culture dishes to subconfluence, rinsed once with 5 ml of ice-cold Ca^{2+}/Mg^{2+}-free phosphate-buffered saline, and scraped into 5 ml of the same buffer. Cells are pelleted by centrifugation (500 x *g*, 5 minutes), resuspended in TEE buffer (25 mM Tris, pH 7.5, 5 mM EDTA, 5 mM EGTA), and frozen in liquid nitrogen. After thawing, the cells are homogenized using a Dounce homogenizer (one ml TEE per plate of cells), and centrifuged at 1,000 x *g* for 5 minutes to remove nuclei and unbroken cells.

The homogenate supernatant is centrifuged at 20,000 x *g* for 20 minutes to isolate the membrane fraction, and the membrane pellet is washed once with TEE and resuspended in binding buffer (20 mM HEPES, pH 7.5, 150 mM NaCl, 10 mM $MgCl_2$, 1 mM EDTA). The resuspended membranes can be frozen in liquid nitrogen and stored at-70°C until use.

Aliquots of cell membranes prepared as described above and stored at -70°C are thawed, homogenized, and diluted into buffer containing 20 mM HEPES, 10 mM $MgCl_2$, 1 mM EDTA, 120 mM NaCl, 10 μM GDP, and 0.2 mM ascorbate, at a concentration of 10-50 μg/ml. In a final volume of 90 μl, homogenates are incubated with varying concentrations of candidate modulator compounds or 100 μM GTP for 30 minutes at 30°C and then placed on ice. To each sample, 10 μl guanosine 5'-O-(3[^{35}S]thio) triphosphate (NEN, 1200 Ci/mmol; [^{35}S]-GTPγS), was added to a final concentration of 100-200 pM.

Samples are incubated at 30°C for an additional 30 minutes, 1 ml of 10mM HEPES, pH 7.4, 10 mM $MgCl_2$, at 4°C is added and the reaction is stopped by filtration.

Samples are filtered over Whatman GF/B filters and the filters are washed with 20 ml ice-cold 10 mM HEPES, pH 7.4, 10 mM $MgCl_2$. Filters are counted by liquid scintillation spectroscopy. Nonspecific binding of [^{35}S]-GTPγS is measured in the presence of 100 μM GTP and subtracted from the total. Compounds are selected that modulate the amount of [^{35}S]-GTPγS binding in the cells, compared to untransfected control cells. Activation of receptors by agonists gives up to a five-fold increase in [^{35}S]GTPγS binding. This response is blocked by antagonists.

G. <u>MAP Kinase Activity Assay</u>

Evaluation of MAP kinase activity in cells expressing a GPCR provides another assay to identify modulators of GPCR activity. (See, *e.g.*, Lajiness *et al.*, Journal of Pharmacology and Experimental Therapeutics 267(3):1573-1581 (1993) and Boulton *et al.*, Cell 65:663-675 (1991).)

In one embodiment, CHO cells stably transfected with nGPCR-x are seeded into 6-well plates at a density of 70,000 cells/well 48 hours prior to the assay. During this 48-hour period, the cells are cultured at 37°C in MEM medium supplemented with 10% fetal bovine serum, 2mM glutamine, 10 U/ml penicillin and 10μg/ml streptomycin. The cells are serum-starved for 1-2 hours prior to the addition of stimulants.

For the assay, the cells are treated with medium alone or medium containing either a candidate agonist or 200 nM Phorbol ester- myristoyl acetate (*i.e*, PMA, a positive control), and the cells are incubated at 37°C for varying times. To stop the reaction, the plates are placed on ice, the medium is aspirated, and the cells are rinsed with 1 ml of ice-cold PBS containing 1mM EDTA. Thereafter, 200μl of cell lysis buffer (12.5 mM MOPS, pH 7.3, 12.5 mM glycerophosphate, 7.5mM $MgCl_2$, 0.5mM EGTA, 0.5 mM sodium vanadate, 1mM benzamidine, 1mM dithiothreitol, 10 μg/ml leupeptin, 10 μg/ml aprotinin, 2μg/ml pepstatin A, and 1μM okadaic acid) is added to the cells. The cells are scraped from the plates and homogenized by 10 passages through a 23 3/4 G needle, and the cytosol fraction is prepared by centrifugation at 20,000 x *g* for 15 minutes.

Aliquots (5-10 μl containing 1-5 μg protein) of cytosol are mixed with 1 mM MAPK Substrate Peptide (APRTPGGRR (SEQ ID NO: 269), Upstate Biotechnology, Inc., N.Y.) and 50μM [γ-^{32}P]ATP (NEN, 3000 Ci/mmol), diluted to a final specific activity of ~2000 cpm/pmol, in a total volume of 25 μl. The samples are incubated for 5 minutes at 30°C, and reactions are stopped by spotting 20 μl on 2 cm^2 squares of Whatman P81 phosphocellulose paper. The filter squares are washed in 4 changes of 1% H_3PO_4, and the squares are subjected to liquid scintillation spectroscopy to quantitate bound label. Equivalent cytosolic extracts are incubated without MAPK substrate peptide, and the bound label from these samples are subtracted from the matched samples with the substrate peptide. The cytosolic extract from each well is used as a separate point. Protein concentrations are determined by a dye binding protein assay (Bio-Rad Laboratories). Agonist activation of the receptor is expected to result in up to a five-fold increase in MAPK enzyme activity. This increase is blocked by antagonists.

H. [^{3}H]Arachidonic Acid Release

The activation of GPCRs also has been observed to potentiate arachidonic acid release in cells, providing yet another useful assay for modulators of GPCR activity. (*See, e.g.*, Kanterman *et al.*, Molecular Pharmacology 39:364-369 (1991).) For example, CHO cells that are stably transfected with a nGPCR-x expression vector are plated in 24-well plates at a density of 15,000 cells/well and grown in MEM medium supplemented with 10% fetal bovine serum, 2 mM glutamine, 10 U/ml penicillin and 10 μg/ml streptomycin for 48 hours at 37°C before use. Cells of each well are labeled by incubation with [^{3}H]-arachidonic acid (Amersham Corp., 210 Ci/mmol) at 0.5 μCi/ml in 1 ml MEM supplemented with 10mM HEPES, pH 7.5, and 0.5% fatty-acid-free bovine serum albumin for 2 hours at 37°C. The cells are then washed twice with 1 ml of the same buffer.

Candidate modulator compounds are added in 1 ml of the same buffer, either alone or with 10μM ATP and the cells are incubated at 37°C for 30 minutes. Buffer alone and mock-transfected cells are used as controls. Samples (0.5 ml) from each well are counted by liquid scintillation spectroscopy. Agonists which activate the receptor will lead to

potentiation of the ATP-stimulated release of [^{3}H]-arachidonic acid. This potentiation is blocked by antagonists.

I. Extracellular Acidification Rate

In yet another assay, the effects of candidate modulators of nGPCR-x activity are assayed by monitoring extracellular changes in pH induced by the test compounds. (*See, e.g.*, Dunlop *et al.*, Journal of Pharmacological and Toxicological Methods 40(1):47-55 (1998).) In one embodiment, CHO cells transfected with a nGPCR-x expression vector are seeded into 12 mm capsule cups (Molecular Devices Corp.) at 4 x 10^5 cells/cup in MEM supplemented with 10% fetal bovine serum, 2 mM L-glutamine, 10 U/ml penicillin, and 10 µg/ml streptomycin. The cells are incubated in this medium at 37°C in 5% CO_2 for 24 hours.

Extracellular acidification rates are measured using a Cytosensor microphysiometer (Molecular Devices Corp.). The capsule cups are loaded into the sensor chambers of the microphysiometer and the chambers are perfused with running buffer (bicarbonate-free MEM supplemented with 4 mM L-glutamine, 10 units/ml penicillin, 10 µg/ml streptomycin, 26 mM NaCl) at a flow rate of 100 µl/minute. Candidate agonists or other agents are diluted into the running buffer and perfused through a second fluid path. During each 60-second pump cycle, the pump is run for 38 seconds and is off for the remaining 22 seconds. The pH of the running buffer in the sensor chamber is recorded during the cycle from 43-58 seconds, and the pump is re-started at 60 seconds to start the next cycle. The rate of acidification of the running buffer during the recording time is calculated by the Cytosoft program. Changes in the rate of acidification are calculated by subtracting the baseline value (the average of 4 rate measurements immediately before addition of a modulator candidate) from the highest rate measurement obtained after addition of a modulator candidate. The selected instrument detects 61mV/pH unit. Modulators that act as agonists of the receptor result in an increase in the rate of extracellular acidification compared to the rate in the absence of agonist. This response is blocked by modulators which act as antagonists of the receptor.

Example 12 - Using nGPCR-x proteins to isolate neurotransmitters

Isolated nGPCR-x proteins of the present invention can be used to isolate novel or known neurotransmitters (Saito *et al.*, Nature 400: 265-269, 1999). The cDNAs that encode the isolated nGPCR-x can be cloned into mammalian expression vectors and used to stably or transiently transfect mammalian cells including CHO, Cos or HEK293 cells. Receptor expression can be determined by Northern blot analysis of transfected cells and identification of an appropriately sized mRNA band (predicted size from the cDNA). Brain regions shown by mRNA analysis to express each of the nGPCR-x proteins could be processed for peptide extraction using any of several protocols ((Reinsheidk R.K. *et al.*, Science 270: 243-247, 1996; Sakurai, T., *et al.*, Cell 92; 573-585, 1998; Hinuma, S., *et al.*, Nature 393: 272-276, 1998). Chromotographic fractions of brain extracts could be tested for ability to activate nGPCR-x proteins by measuring second messenger production such as changes in cAMP production in the presence or absence of forskolin, changes in inositol 3-phosphate levels, changes in intracellular calcium levels or by indirect measures of receptor activation including receptor stimulated mitogenesis, receptor mediated changes in extracellular acidification or receptor mediated changes in reporter gene activation in response to cAMP or calcium (these methods should all be referenced in other sections of the patent). Receptor activation could also be monitored by co-transfecting cells with a chimeric $GI_{q/i3}$ to force receptor coupling to a calcium stimulating pathway (Conklin *et al.*, Nature 363; 274-276, 1993). Neurotransmitter mediated activation of receptors could also be monitored by measuring changes in $[^{35}$ S]-GTPKS binding in membrane fractions prepared from transfected mammalian cells. This assay could also be performed using baculoviruses containing nGPCR-x proteins infected into SF9 insect cells.

The neurotransmitter which activates nGPCR-x proteins can be purified to homogeneity through successive rounds of purification using nGPCR-x proteins activation as a measurement of neurotransmitter activity. The composition of the neurotransmitter can be determined by mass spectrometry and Edman degradation if peptidergic. Neurotransmitters isolated in this manner will be bioactive materials which will alter

neurotransmission in the central nervous system and will produce behavioral and biochemical changes.

Example 13 - Using nGPCR-x proteins to isolate and purify G proteins

cDNAs encoding nGPCR-x proteins are epitope–tagged at the amino terminuus end of the cDNA with the cleavable influenza-hemagglutinin signal sequence followed by the FLAG epitope (IBI, New Haven, CT). Additionally, these sequences are tagged at the carboxyl terminus with DNA encoding six histidine residues. (Amino and Carboxyl Terminal Modifications to Facilitate the Production and Purification of a G Protein-Coupled Receptor, B.K. Kobilka , *Analytical Biochemistry*, Vol. 231, No. 1, Oct 1995, pp. 269-271). The resulting sequences are cloned into a baculovirus expression vector such as pVL1392 (Invitrogen). The baculovirus expression vectors are used to infect SF-9 insect cells as described (Guan, X. M., Kobilka, T. S., and Kobilka, B. K. (1992) *J. Biol. Chem.* **267**, 21995-21998). Infected SF-9 cells could be grown in 1000-ml cultures in SF900 II medium (Life Technologies, Inc.) containing 5% fetal calf serum (Gemini, Calabasas, CA) and 0.1 mg/ml gentamicin (Life Technologies, Inc.) for 48 hours at which time the cells could be harvested. Cell membrane preparations could be separated from soluble proteins following cell lysis. nGPCR-x protein purification is carried out as described for purification of the ϑ2 receptor (Kobilka, Anal. Biochem., 231 (1): 269-271, 1995) including solubilization of the membranes in 0.8-1.0 % *n*-dodecyl -D-maltoside (DM) (CalBiochem, La Jolla, CA) in buffer containing protease inhibitors followed by Ni-column chromatography using chelating Sepharose™ (Pharmacia, Uppsala, Sweden). The eluate from the Ni-column is further purified on an M1 anti-FLAG antibody column (IBI). Receptor containing fractions are monitored by using receptor specific antibodies following western blot analysis or by SDS-PAGE analysis to look for an appropriate sized protein band (appropriate size would be the predicted molecular weight of the protein).

This method of purifying G protein is particularly useful to isolate G proteins that bind to the nGPCR-x proteins in the absence of an activating ligand.

EXAMPLE 14: CLONE DEPOSIT INFORMATION

In accordance with the Budapest Treaty, clones of the present invention have been deposited at the Agricultural Research Culture Collection (NRRL) International Depository Authority, 1815 N. University Street, Peoria, Illinois 61604, U.S.A. Accession numbers and deposit dates are provided below in Table 6.

Table 6: DEPOSIT INFORMATION

Clone	Accession Number NRRL	Budapest Treaty Deposit Date
nGPCR-74 (SEQ ID NO:134)	UC20088	2000 Feb 22

Some of the preferred embodiments of the invention described above are outlined below and include, but are not limited to, the following embodiments. As those skilled in the art will appreciate, numerous changes and modifications may be made to the preferred embodiments of the invention without departing from the spirit of the invention. It is intended that all such variations fall within the scope of the invention.

The entire disclosure of each publication cited herein is hereby incorporated by reference.

What is claimed is:

1. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence homologous to sequences selected from the group consisting of: SEQ ID NO:135 to SEQ ID NO:268; said nucleic acid molecule encoding at least a portion of nGPCR-x.

2. The isolated nucleic acid molecule of claim 1 comprising a sequence that encodes a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268.

3. The isolated nucleic acid molecule of claim 1 comprising a sequence homologous to a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134.

4. The isolated nucleic acid molecule of claim 1 comprising a sequence selected from the group of sequences consisting of SEQ ID NO:1 to SEQ ID NO:134.

5. The isolated nucleic acid molecule of claim 1 wherein said nucleic acid molecule is DNA.

6. The isolated nucleic acid molecule of claim 1 wherein said nucleic acid molecule is RNA.

7. An expression vector comprising a nucleic acid molecule of any one of claims 1 to 4.

8. The expression vector of claim 7 wherein said nucleic acid molecule comprises a sequence selected from the group of sequences consisting of SEQ ID NO:1 to SEQ ID NO:134.

9. The expression vector of claim 7 wherein said vector is a plasmid.

10. The expression vector of claim 7 wherein said vector is a viral particle.

11. The expression vector of claim 10 wherein said vector is selected from the group consisting of adenoviruses, baculoviruses, parvoviruses, herpesviruses, poxviruses, adeno-associated viruses, Semliki Forest viruses, vaccinia viruses, and retroviruses.

12. The expression vector of claim 7 wherein said nucleic acid molecule is operably connected to a promoter selected from the group consisting of simian virus 40, mouse mammary tumor virus, long terminal repeat of human immunodeficiency virus, maloney virus, cytomegalovirus immediate early promoter, Epstein Barr virus, rous sarcoma virus, human actin, human myosin, human hemoglobin, human muscle creatine, and human metalothionein.

13. A host cell transformed with an expression vector of claim 7.

14. The transformed host cell of claim 13 wherein said cell is a bacterial cell.

15. The transformed host cell of claim 14 wherein said bacterial cell is E. coli.

16. The transformed host cell of claim 13 wherein said cell is yeast.

17. The transformed host cell of claim 16 wherein said yeast is S. cerevisiae.

18. The transformed host cell of claim 13 wherein said cell is an insect cell.

19. The transformed host cell of claim 18 wherein said insect cell is S. frugiperda.

20. The transformed host cell of claim 13 wherein said cell is a mammalian cell.

21. The transformed host cell of claim 20 wherein mammalian cell is selected from the group consisting of chinese hamster ovary cells, HeLa cells, African green monkey kidney cells, human HEK-293 cells, and murine 3T3 fibroblasts.

22. An isolated nucleic acid molecule comprising at least 10 nucleotides, said isolated nucleic acid comprising a nucleotide sequence complementary to a sequence selected from the group of sequences consisting of SEQ ID NO:1 to SEQ ID NO:134.

23. The nucleic acid molecule of claim 22 wherein said molecule is an antisense oligonucleotide directed to a region of a sequence selected from the group of sequences consisting of SEQ ID NO:1 to SEQ ID NO:134.

24. The nucleic acid molecule of claim 23 wherein said oligonucleotide is directed to a regulatory region of a sequence selected from the group of sequences consisting of SEQ ID NO:1 to SEQ ID NO:134.

25. A composition comprising a nucleic acid molecule of any one of claims 1 to 4 or 22 and an acceptable carrier or diluent.

26. A composition comprising a recombinant expression vector of claim 7 and an acceptable carrier or diluent.

27. A method of producing a polypeptide that comprises a sequence selected from the group of sequences consisting SEQ ID NO:135 to SEQ ID NO:268, and homologs thereof, said method comprising the steps of:

a) introducing a recombinant expression vector of claim 8 into a compatible host cell;

b) growing said host cell under conditions for expression of said polypeptide; and

c) recovering said polypeptide.

28. The method of claim 27 wherein said host cell is lysed and said polypeptide is recovered from the lysate of said host cell.

29. The method of claim 27 wherein said polypeptide is recovered by purifying the culture medium without lysing said host cell.

30. An isolated polypeptide encoded by a nucleic acid molecule of claim 1.

31. The polypeptide of claim 30 wherein said polypeptide comprises a sequence selected from the group of sequences consisting of SEQ ID NO:135 to SEQ ID NO:268.

32. The polypeptide of claim 30 wherein said polypeptide comprises an amino acid sequence homologous to a sequence selected from the group of sequences consisting of SEQ ID NO:135 to SEQ ID NO:268.

33. The polypeptide of claim 30 wherein said sequence homologous to a sequence selected from the group of sequences consisting of SEQ ID NO:135 to SEQ ID NO:268 comprises at least one conservative amino acid substitution compared to the sequences in the group of sequences consisting of SEQ ID NO:135 to SEQ ID NO:268.

34. The polypeptide of claim 30 wherein said polypeptide comprises an allelic variant of a polypeptide with a sequence selected from the group of sequences consisting of SEQ ID NO:135 to SEQ ID NO:268.

35. A composition comprising a polypeptide of claim 34 and an acceptable carrier or diluent.

36. An isolated antibody which binds to an epitope on a polypeptide of claim 30.

37. The antibody of claim 36 wherein said antibody is a monoclonal antibody.

38. A composition comprising an antibody of claim 36 and an acceptable carrier or diluent.

39. A method of inducing an immune response in a mammal against a polypeptide of claim 30 comprising administering to said mammal an amount of said polypeptide sufficient to induce said immune response.

40. A method for identifying a compound which binds nGPCR-x comprising the steps of:

a) contacting nGPCR-x with a compound; and

b) determining whether said compound binds nGPCR-x.

41. The method of claim 40 wherein the nGPCR-x comprises an amino acid sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268.

42. The method of claim 40 wherein binding of said compound to nGPCR-x is determined by a protein binding assay.

43. The method of claim 40 wherein said protein binding assay is selected from the group consisting of a gel-shift assay, Western blot, radiolabeled competition assay, phage-based expression cloning, co-fractionation by chromatography, co-precipitation, cross linking, interaction trap/two-hybrid analysis, southwestern analysis, and ELISA.

44. A compound identified by the method of claim 40.

45. A method for identifying a compound which binds a nucleic acid molecule encoding nGPCR-x comprising the steps of:

a) contacting said nucleic acid molecule encoding nGPCR-x with a compound; and

b) determining whether said compound binds said nucleic acid molecule.

46. The method of claim 45 wherein binding is determined by a gel-shift assay.

47. A compound identified by the method of claim 45.

48. A method for identifying a compound which modulates the activity of nGPCR-x comprising the steps of:

a) contacting nGPCR-x with a compound; and

b) determining whether nGPCR-x activity has been modulated.

49. The method of claim 48 wherein the nGPCR-x comprises an amino acid sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268.

50. The method of claim 48 wherein said activity is neuropeptide binding.

51. The method of claim 48 wherein said activity is neuropeptide signaling.

52. A compound identified by the method of claim 48.

53. A method of identifying an animal homolog of nGPCR-x comprising the steps:

a) comparing the nucleic acid sequences of the animal with a sequence selected from the group of sequence consisting of SEQ ID NO:1 to SEQ ID NO:134, and portions thereof, said portions being at least 10 nucleotides; and

b) identifying nucleic acid sequences of the animal that are homologous to said sequence selected from the group sequence consisting of SEQ ID NO:1 to SEQ ID NO:134, and portions thereof, said portions comprising at least 10 nucleotides.

54. The method of claim 53 wherein comparing the nucleic acid sequences of the animal with a sequence selected from the group of sequences consisting of SEQ ID NO:1

to SEQ ID NO:134, and portions thereof, said portions being at least 10 nucleotides, is performed by DNA hybridization.

55. The method of claim 53 wherein comparing the nucleic acid sequences of the animal with a sequence selected from the group of sequences consisting of SEQ ID NO:1 to SEQ ID NO:134, and portions thereof, said portions being at least 10 nucleotides, is performed by computer homology search.

56. A method of screening a human subject to diagnose a disorder affecting the brain or genetic predisposition therefor, comprising the steps of:

(a) assaying nucleic acid of a human subject to determine a presence or an absence of a mutation altering an amino acid sequence, expression, or biological activity of at least one nGPCR-x that is expressed in the brain, wherein the nGPCR-x comprises an amino acid sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, and allelic variants thereof, and wherein the nucleic acid corresponds to a gene encoding the nGPCR-x; and

(b) diagnosing the disorder or predisposition from the presence or absence of said mutation, wherein the presence of a mutation altering the amino acid sequence, expression, or biological activity of the nGPCR-x in the nucleic acid correlates with an increased risk of developing the disorder.

57. A method according to claim 56, wherein the disease is a mental disorder.

58. A method according to claim 56, wherein the assaying step comprises at least one procedure selected from the group consisting of:

a) comparing nucleotide sequences from the human subject and reference sequences and determining a difference of at least a nucleotide of at least one codon between the nucleotide sequences from the human subject that encodes a nGPCR-x reference sequence;

(b) performing a hybridization assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences;

(c) performing a polynucleotide migration assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences; and

(d) performing a restriction endonuclease digestion to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences.

59. A method according to claim 58 wherein the assaying step comprises: performing a polymerase chain reaction assay to amplify nucleic acid comprising nGPCR-x coding sequence, and determining nucleotide sequence of the amplified nucleic acid.

60. A method of screening for an nGPCR-x hereditary mental disorder genotype in a human patient, comprising the steps of:

(a) providing a biological sample comprising nucleic acid from said patient, said nucleic acid including sequences corresponding to alleles of nGPCR-x; and

(b) detecting the presence of one or more mutations in the nGPCR-x allele;

wherein the presence of a mutation in a nGPCR-x allele is indicative of a hereditary mental disorder genotype.

61. The method according to claim 60 wherein said biological sample is a cell sample.

62. The method according to claim 60 wherein said detecting the presence of a mutation comprises sequencing at least a portion of said nucleic acid, said portion comprising at least one codon of said nGPCR-x allele, said portion comprising at least 10 nucleotides.

63. The method according to claim 60 wherein said nucleic acid is DNA.

64. The method according to claim 60 wherein said nucleic acid is RNA.

65. A kit for screening a human subject to diagnose a mental disorder or a genetic predisposition therefor, comprising, in association:

(a) an oligonucleotide useful as a probe for identifying polymorphisms in a human nGPCR-x gene, the oligonucleotide comprising 6-50 nucleotides in a sequence that is identical or complementary to a sequence of a wild type human nGPCR-x gene sequence or nGPCR-x coding sequence, except for one sequence difference selected from the group consisting of a nucleotide addition, a nucleotide deletion, or nucleotide substitution; and

(b) a media packaged with the oligonucleotide, said media containing information for identifying polymorphisms that correlate with mental disorder or a genetic predisposition therefor, the polymorphisms being identifiable using the oligonucleotide as a probe.

66. A method of identifying a nGPCR-x allelic variant that correlates with a mental disorder, comprising the steps of:

(a) providing a biological sample comprising nucleic acid from a human patient diagnosed with a mental disorder, or from the patient's genetic progenitors or progeny;

(b) detecting in the nucleic acid the presence of one or more mutations in an nGPCR-x that is expressed in the brain, wherein the nGPCR-x comprises an amino acid sequence selected from the group consisting of SEQ ID NO:135 to SEQ ID NO:268, and allelic variants thereof, and wherein the nucleic acid includes sequence corresponding to the gene or genes encoding nGPCR-x;

wherein the one or more mutations detected indicates an allelic variant that correlates with a mental disorder.

67. A purified and isolated polynucleotide comprising a nucleotide sequence encoding a nGPCR-x allelic variant identified according to claim 66.

68. A host cell transformed or transfected with a polynucleotide according to claim 67 or with a vector comprising the polynucleotide.

69. A purified polynucleotide comprising a nucleotide sequence encoding nGPCR-x of a human with a mental disorder;

wherein said polynucleotide hybridizes to the complement of a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134 under the following hybridization conditions:

(a) hybridization for 16 hours at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaCl, 10% dextran sulfate and

(b) washing 2 times for 30 minutes at 60°C in a wash solution comprising 0.1x SSC and 1% SDS; and

wherein the polynucleotide that encodes nGPCR-x amino acid sequence of the human differs from the sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134 by at least one residue.

70. A vector comprising a polynucleotide according to claim 69.

71. A host cell that has been transformed or transfected with a polynucleotide according to claim 69 and that expresses the nGPCR-x protein encoded by the polynucleotide.

72. A host cell according to claim 71 that has been co-transfected with a polynucleotide encoding the nGPCR-x amino acid sequence set forth in a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:134 and that expresses the nGPCR-x protein having the amino acid sequence set forth in SEQ ID NO:135 to SEQ ID NO:268.

73. A method for identifying a modulator of biological activity of nGPCR-x comprising the steps of:

a) contacting a cell according to claim 72 in the presence and in the absence of a putative modulator compound;

b) measuring nGPCR-x biological activity in the cell;

wherein decreased or increased nGPCR-x biological activity in the presence versus absence of the putative modulator is indicative of a modulator of biological activity.

74. A method to identify compounds useful for the treatment of a mental disorder, said method comprising the steps of:

(a) contacting a composition comprising nGPCR-x with a compound suspected of binding nGPCR-x;

(b) detecting binding between nGPCR-x and the compound suspected of binding nGPCR-x;

wherein compounds identified as binding nGPCR-x are candidate compounds useful for the treatment of a mental disorder.

75. A method for identifying a compound useful as a modulator of binding between nGPCR-x and a binding partner of nGPCR-x comprising the steps of:

(a) contacting the binding partner and a composition comprising nGPCR-x in the presence and in the absence of a putative modulator compound;

(b) detecting binding between the binding partner and nGPCR-x;

wherein decreased or increased binding between the binding partner and nGPCR-x in the presence of the putative modulator, as compared to binding in the absence of the putative modulator is indicative a modulator compound useful for the treatment of a mental disorder.

76. A method according to claim 74 or 75 wherein the composition comprises a cell expressing nGPCR-x on its surface.

77. A method according to claim 76 wherein the composition comprises a cell transformed or transfected with a polynucleotide that encodes nGPCR-x.

78. A method of purifying a G protein from a sample containing said G protein comprising the steps of:

a) contacting said sample with a polypeptide of claim 1 for a time sufficient to allow said G protein to form a complex with said polypeptide;

b) isolating said complex from remaining components of said sample;

c) maintaining said complex under conditions which result in dissociation of said G protein from said polypeptide; and

d) isolating said G protein from said polypeptide.

79. The method of claim 78 wherein said sample comprises an amino acid sequence selected from the group of sequences consisting of SEQ ID NO:135 to SEQ ID NO:268.

80. The method of claim 78 wherein said polypeptide comprises an amino acid sequence homologous to a sequence selected from the group of sequences consisting of SEQ ID NO:135 to SEQ ID NO:268.

81. The method of claim 78 wherein said polypeptide comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:135 to SEQ ID NO:268.

82. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence homologous a sequence of SEQ ID NO:268; said nucleic acid molecule encoding at least a portion of nGPCR-x.

83. The isolated nucleic acid molecule of claim 82 comprising a sequence that encodes a polypeptide comprising a sequence of SEQ ID NO:268.

84. The isolated nucleic acid molecule of claim 82 comprising a sequence homologous to a sequence of SEQ ID NO:134.

85. The isolated nucleic acid molecule of claim 82 comprising a sequence of SEQ ID NO:134.

86. An expression vector comprising a nucleic acid molecule of any one of claims 82 to 85.

87. A host cell transformed with an expression vector of claim 86.

88. An isolated polypeptide encoded by a nucleic acid molecule of claim 82.

89. The polypeptide of claim 88 wherein said polypeptide comprises a sequence of SEQ ID NO:268.

90. The polypeptide of claim 88 wherein said polypeptide comprises an amino acid sequence homologous to a sequence of SEQ ID NO:268.

91. An isolated antibody which binds to an epitope on a polypeptide of claim 88.

92. A method for identifying a compound which binds nGPCR-x comprising the steps of:

a) contacting nGPCR-x with a compound; and

b) determining whether said compound binds nGPCR-x.

93. A method for identifying a compound which modulates the activity of nGPCR-x comprising the steps of:

a) contacting nGPCR-x with a compound; and

b) determining whether nGPCR-x activity has been modulated.

94. The method of claim 93 wherein the nGPCR-x comprises an amino acid sequence of SEQ ID NO:268.

95. A method of screening a human subject to diagnose a disorder affecting the brain or genetic predisposition therefor, comprising the steps of:

(a) assaying nucleic acid of a human subject to determine a presence or an absence of a mutation altering an amino acid sequence, expression, or biological activity of at least one nGPCR-x that is expressed in the brain, wherein the nGPCR-x comprises an amino acid sequence of SEQ ID NO:268, and allelic variants thereof, and wherein the nucleic acid corresponds to a gene encoding the nGPCR-x; and

(b) diagnosing the disorder or predisposition from the presence or absence of said mutation, wherein the presence of a mutation altering the amino acid sequence, expression, or biological activity of the nGPCR-x in the nucleic acid correlates with an increased risk of developing the disorder.

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<110> Pharmacia & Upjohn Company
Vogeli, Gabriel
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<213> Homo sapiens

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<212> DNA
<213> Homo sapiens

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<211> 462

<212> DNA
<213> Homo sapiens

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<210> 23
<211> 692
<212> DNA
<213> Homo sapiens

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tctgccaaac ataggccaaa attcatctcc ttggtttgca ggtacagttt gtctaatcct 240

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<211> 669
<212> DNA
<213> Homo sapiens

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agaggactgt ggtttgatga gttcattcat gccgtggctt taattactga taagagcttg 180

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<211> 654
<212> DNA
<213> Homo sapiens

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aataaaatcc aaatttaatc catcacattg acaatgatta aaattaaatt taaagcagtg 180
ttgggaagaa tacagtgagc tggtgtccat acacactgtg atgagagtgt agaaatctta 240
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caatttttgc cttggaaaaa tatggtatca ctacagaaat gttgtagtgt tatcgctgac 600
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<210> 26
<211> 687
<212> DNA
<213> Homo sapiens

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gggactgttg cgctggactt gacaggtgaa ctgaaaattg cagggataag tacacctatt 480

gagaacaaac atcccatctc tttatcaaag ctcttcattg gctttggaaa actgctgtag 540

gcctaaggaa actaaacttt ctagggatat tctaggtttt aaacatatga gaaagagaaa 600

gacgtcggtt cttatttaag agagtttatg agaccttatc cttgaaatag tcaaatttat 660

aaatgacata aggctgtatg tgtagtt 687

<210> 27
<211> 622
<212> DNA
<213> Homo sapiens

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cttgcccatt tgtgtacact catcttgtgc tactctcttt cttcatcaat atgctccacc 180

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aattctccaa gcatcgtatc ctctgtgttc ctatagcact acattggatc ggtccataac 480

aattctgtca gtgtattata agaacttatt tacaggtttt gtctcttcta ctatggcgtg 540

agccttttag tcatatgaat tgtgattttg tatatttagc gcctaccatg gtgcttaatt 600

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<212> DNA
<213> Homo sapiens

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aaaacaaaac aaaatgttta acctgaaacc cttacaaaac acgtaaaatt tatatttaaa 540

aaatctaaat atttgaggag agaacgaaac ctaagtatat gcccaggtat aacacgattg 600

gtggagatag ctttaaaaaa gttcctgaaa aatttagttt ttaaaagggt accctagtag 660

aaggtgactt aactgcctaa tttc 684

<210> 29
<211> 731
<212> DNA
<213> Homo sapiens

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ccccaggagt ttccagacag ctgcacagat ttaagtgcag aaatctgagc agaggtatag 180

tcctggcatt tacatgaaca cctttcagta gcaggaagaa taaatggaaa gagagctaca 240

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cacagaggga ggattagctg gagaagcagg acagagggca agagagacga gatctccgac 660

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<213> Homo sapiens

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acaaatttca aggagaaatt ttaaaaggag agtaacaaac tgtcctgagt tgcagcaaga 360

ctcctgagag ttccatttcc tgggccctct gctgcctgtt tttggcattg aacccaggaa 420

tcttttctaa agcacacaga aatcttgcaa aagaggccat ttctagttag gcttttgtcc 480

aactgtctag ttaaataaat taaattctta gattacaaaa tgtgcttcaa aggtttaaca 540

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tctactttcc tcttccacac ctatgatgaa tgtcctgaaa ag 642

<210> 31
<211> 592
<212> DNA
<213> Homo sapiens

<400> 31
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<211> 485
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<213> Homo sapiens

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tcacaaacgc aacaaatact tactgagcac ctactctgtg ccaggtgctg tgctatatgc 180

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ggatctgaag actgagagtt atctaagtgg ggagagcatt gcaggcaggg ggatcagcat 420

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<212> DNA
<213> Homo sapiens

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<211> 506
<212> DNA
<213> Homo sapiens

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<213> Homo sapiens

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<210> 37
<211> 563
<212> DNA
<213> Homo sapiens

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<210> 38
<211> 604
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<210> 39
<211> 687
<212> DNA
<213> Homo sapiens

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gttatgcggg catcagggca acatggggag aacagtggca ggcacataag gccacccccca 180

ggtacaatgt ccagtgcagt tcacgggtag gtaaatctac tctgtgtccc cacagaccca 240

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<211> 550

<212> DNA
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caccatttaa gaaagagaga aaataaaaat gctcatttct aattgtcctc atttcagcag 480

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<210> 41
<211> 617
<212> DNA
<213> Homo sapiens

<400> 41
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caaattgtta cttgctagct taggaaagaa tccttggaaa tccaacatat tgtctaaatg 240

gatcagttaa tcttactatg tgcattctac ataccctttc attgtttggg cttaaataac 300

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gttttagaat agaaacagtt ctgagatgaa gttgagcaca atttcctgtt ctagttgcaa 420

ttaaatataa atatagcatt tgacataaaa tagctggccc gatatattta gagtacaagt 480

taagtgtcat ccccttagaa ttgggcattg actccgtaga attccccttt gtacaaggtg 540

agcaaatgta tattttgtta aaaataagta tctgactgcc aaaacggaca gaaagctctt 600

tgccatatgt gttttca 617

<210> 42
<211> 653
<212> DNA
<213> Homo sapiens

<400> 42
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gtttttctta cccgtggaga ggtgtattct tgaacccttt aaacgggtct ctactttggc 240

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ttatatggta tattctccca ttacatttta gccacaatgc ccgtatatta aataagcaaa 360

caaactatat gtggcaatta aaacttaaaa aaaaaagcct gaattggctc ttagaaatat 420

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tacccaaccc tgctgtcatt cagggtccta gcaggaacag gtagcatcaa ataggataat 540

tgatgagagc ttaagaaagg aactatttac aaatatgtgg ccagattagg ggaaaccagt 600

aaggttggga atgccgccca ggattctaac aagagtgaga atctatttct act 653

<210> 43
<211> 642
<212> DNA
<213> Homo sapiens

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aactagtaat gaccccaaaa aggtttttta taatatgaat tttatatata aatattttat 180

tggaagtcca cttttatgaa aataaccttt tttcaaaaat ttcataagaa aaaaatagta 240

ttattttaca tatttgaggc atctttttaa tgcctggttt aatagaagac aattgaatat 300

tcatgtcaac ttctggattc gatctgtttc aatatgtgtc tttggttgaa atacatgaag 360

gaaacttggg atcatcagac atatagttag aaaagggtgg agtattttaa cagccttttt 420

ggacaactgt ggacattgtg ctttgatatt acaacaaaac tggagaagtg gtaggttcta 480

aatgattagt tgcaacatgg aatctgaaac cacatcatga actatttgta atctggcata 540

ttaagatcta tttatctatc ttgcactttg aatgggatcc tttgctcatg catctttttg 600

taacatgaat catctcaaac acgttggttc attgagttat gc 642

<210> 44
<211> 674
<212> DNA
<213> Homo sapiens

<400> 44
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cttgaaagga gaagacaagc aatttgggga gataacagca ccagaaattg agttcatctg 180

taacttaggc tctctgtgag tttgtttacc agctattcac catgtggatg aaaaacagta 240

aaaagacaaa aaagattcac atttcaaggc tccctaaaat tgccaattcc actctatagc 300

tgattctcag cacaggagga aatgggacta gaatgctggg agatgacact atcatcgaac 360

agtgagctcc aaggagaagc ctaattgtta cttctcaatg gcagaaggcg ggtgcttccc 420

ccggggcagg attctgttta atccttaggt tagagcccag cttcaaccca gtgtcacagg 480

tcaattacca ccctccaacc ctgaggggcg acatgaacca tactcacgca ccggcgcatg 540

ctccctcctc agcacctctt gtacattcag agctcctgca tgggatgccg agaactcaca 600

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gtcaacaacg acac 674

<210> 45
<211> 609
<212> DNA
<213> Homo sapiens

<400> 45
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ttggaggaca tttgttgaaa actccacact tccatgaggt ctgtagcctt gagcctatca 180

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gcttttaact ataattcaca gagtcctttg aacacataaa gggaaagcca ctttcgctcc 360

tgttaaggat gtataagcac aaaaaatgaa cagtgaatta atcctagtgt tttatacatt 420

ttttttaaa aaaagaatct aagccagaat gaggttactg cctaggcaaa gaagaagaca 480

gctcatcaca ggtgagtgta acacgttttt catatgtaca aattaagcag cctgaaacaa 540

aaggcactca aaaggtaaaa gaataccagt ccacccctct gatttgtcaa atcaaagttc 600

tgtcaactg 609

<210> 46
<211> 522
<212> DNA
<213> Homo sapiens

<400> 46
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atgattaaag tgtacggagg aatgtgcata ggttatatgc caatactgcc tcattttata 180

tgagggactt gaacatagaa gggttttgga gtccacagag gtcctgaaac caatttcccc 240

ttcccatgcc tgggatgact gaattataca gcagcaaaaa tgaatatact caagctatat 300

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gttgatatat aaaggtgcta aacacagaac tatttaatga tatacggatg cagtaaaagt 420

ataagaaatg tatgcaaact tacttaaatt cagggtgttg gttacttgga gtaaggcgaa 480

tgtttgggat gtcagtaggt acctgacaaa tggcaactta ac 522

<210> 47
<211> 681
<212> DNA
<213> Homo sapiens

<400> 47
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ctcttatttt aaactcactt aacatcaata taaaagtgtc ctttgcagca ggacactttt 180

aggaggtctt gagcccctct cccaccagca ctcatctgtg tacaaacaag ttgttgctag 240

tggtgttgga gctcgttttt cccaagcttc accttggcat tacccagatc tgttcaaccc 300

tgggcatctc ttcctcccag ctggatgctc acccaacttg ttctgcctca gtttctggag 360

gagcctgact ctatttttgc ccccttgaa agaaagtaca ggactgggtt gaggcagctg 420

ctcacactca ccagaggcct ccatatcttg taggccacac tggctgccat caagagctgg 480

cagtcctgag aaagcagaaa gcagatggtg aggtagaagg agcgagtgat atggaagggc 540

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gctgtgttgc ctgtcctcat gaggttctcc tctggcttga tcaggctcct gaccatcagt 660

gaatagcaca ccaaagtgac c 681

<210> 48
<211> 548
<212> DNA
<213> Homo sapiens

<400> 48
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ccgagcccag cacagctgcc ctctggaccc tgcggacccc agccgagccc cttcctgagt 120

tccacaggcg cagccccggg gcggtcgggc ggaggggtcc ccggggcggt gccagggcgc 180

aatcctggag ggcggccggg aggaggaggt gcgcgcggcc atgcacaccg tggctacgtc 240

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ctgccgccac aagccgatgc ggaccgtgac caacttctac atcggtgagt gcgggccgct 480

gcgccgcacc tgctgccgtc ccggggggct ccgagggccg agcggcctgg ggcgccctct 540

cgcgacgc 548

<210> 49
<211> 695
<212> DNA
<213> Homo sapiens

<400> 49
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tatatttctc ttgctgtcag gttacccctt ggtatacctg taattgattt ccccagttag 120

agagtttaga tgtggacagg ggaagtacaa actacagctt agtgcaagat aaaccaaggg 180

tgtaattatc aagttgtact tgaacagaaa tattacccaa taggatttcc aaatgaacag 240

gatggcaaag agttctgggg tgtggaagtc agagtaggtg ccaaaggatc tagatcaaag 300

gggttggtag atgagcaggg atgggtcaga gaaatctagg actgttaaag caagcatgac 360

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aaaaacatgg tatatggcat atttgaggag caaagataag ttcattgtca ctagggcaga 540

gcaagggata agtgaatggt gtgagacaag attggagagg ttaacagtgg ccaataacaa 600

gtgataaaaa taattttcaa atgagagcag cccagcactt ataaagtggt taatgtgcac 660

caagtactgc tttaagttat cctgcagtat tattg 695

<210> 50
<211> 586
<212> DNA
<213> Homo sapiens

<400> 50
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tgtagtatag taaatgggcc atctcaaatt gtatctctat cccagtgctc ttctcctaga 120

cctcttgcac cacctactcc acatgtaaga ccttctacat tttggttgtg ttgttcatca 180

tcttcacaca ttgcccaaca agaacatcca gaagccatca tcacagcacc actgcccagg 240

tcatcacagc tcactcttct tcctcaaccc cagcctccat gagaggcaaa ggcgcttaac 300

tggctctcct ctgcttgtta atcacatgaa aatcaagcat gcttatagtg tcctagtaca 360

acaggaaatt tactttcaaa caaggaaagc cacagaaacc ctggggatca ttttaggggc 420

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ttaagacatc ttcatcttgc tgagcttttt tttttttttc tttttgatac caagtctcac 540

tcttgtctcc caggctagaa tgcaatggta caatctcagc tcactg 586

<210> 51
<211> 234
<212> DNA
<213> Homo sapiens

<400> 51
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aaagcaaagt ggcacctcgc aaacaccctg tggccccaag tagtctcacc caaccttggg 120

gaagaagcag aattcaagct gtaactgcct gttggagaga gccaaccctc ggcctctgtc 180

ctcgaaaggc agcaccaaag ttttccaagt ggaatcaaat gtgcagggag gatc 234

<210> 52
<211> 308
<212> DNA
<213> Homo sapiens

<400> 52
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acgtgtactg agcattgtcc taggtatttg agatacatca gtgaacagag gatccttaac 120

agacaatata cataataagt tatgtaatag cttacaaagt gacagtacct ttgggaaaaa 180

ggaaaggtat tataggataa agatgatcaa tgaacaggaa gtttgcagtt ttaaattgag 240

tggtctgggt aaggaagatc atacctgaac caagacacaa aggaggttag ggaatgatga 300

gccctgca 308

<210> 53
<211> 584
<212> DNA
<213> Homo sapiens

<400> 53
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gcatgaatgt ggaaatgaaa ggggatgcag atggagatga tgcagatgga gatgatgatg 120

cagatggaga tgatgcagat ggagatgatg cagatggaga gcagtggcca tgcagagtct 180

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acctccagtg cttgccagca atgccacctt gggtgacctt tatcttgcta cctggaaagt 300

ggggatgctg gcagcccctc cctcctggca tcactgacac tgcatggtca gggtgtgatc 360

cctttgggta caggcggggg tggtggacct cccaggtggg caggtccagt ttggatgaaa 420

ggccaaggac gattcatagg agagcacagg agtccttgct tagccccagc aattccacag 480

aacctgctgt gaactgctgg ctgctgcccg taacttttcc ctgtccctat ttccactcct 540

tggaggccgc aagaacaact gctggctggc cttggccact gcct 584

<210> 54
<211> 560
<212> DNA
<213> Homo sapiens

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ctgtataaaa gattatgtca ccagaatctt ctttcattac tttggatagg acctaaagga 180

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tccagaatat taatttagtt ctattcattg actattcttt ggttttgctg ttgaattttt 480

aaattcagga atagtgtgtt tttctttcag attatttttt tctgtgacct aattgcatct 540

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<210> 55
<211> 234
<212> DNA
<213> Homo sapiens

<400> 55
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ctgcctaaac ccactcctgt actttctttc aaggggggca aaatttgagt caggctcctc 180

cagaaactga ggcagaacaa gttgggtgag catccagctg ggaggaagag atgc 234

<210> 56
<211> 585
<212> DNA
<213> Homo sapiens

<400> 56
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taacctcatg aggtacaggc aacacagccc gagccaggtc catccgggac catcctactg 120

gtgtgtggcc tcttcaccct ctgttttgtg cccttccata tcactcgctc cttctacctc 180

accatctgct ttctgctttc tcaggactgc cagctcttga tggcagccag tgtggcctac 240

aagatatgga ggcctctggt gagtgtgagc agctgcctca acccagtcct gtactttctt 300

tcaagggggg caaaaataga gtcaggctcc tccagaaact gaggcagaac aagttgggtg 360

agcatccagc tgggaggaag agatgcccag ggttgaacag atctgggtaa tgccaaggtg 420

aagcttggga aaaacgagct ccaacaccac tagcaacaac ttgtttgtac acagatgagt 480

gctggtggga gaggggctca agacctccta aaagtgtcct gctgcaaagg acacttttat 540

attgatgtta agtgagttta aaataagagt atggagagag ccact 585

<210> 57
<211> 660
<212> DNA
<213> Homo sapiens

<400> 57
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agaatgtggc tcagagactt ccatctatgg ggaactcaat caaccaaagg ccccagctcc 540

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agccaatgcc caaacaatgg cagggagact aaggcatcct gttcctgggg agatgtggga 660

<210> 58
<211> 643
<212> DNA
<213> Homo sapiens

<400> 58
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<211> 670
<212> DNA
<213> Homo sapiens

<400> 59
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tcaagataaa ataatttttt ccatttattg acccattttt agcttacaat ttgttttcta 360

cccttgtaag tattatgttt ggtaaattat tttttattaa tatctccctt acagatatta 420

tacgccataa ggaaaggagt cacagatttg gtaatagaga ctcaatacac gtttgttgga 480

atgatgaaag cattatgagg catattttct tactatgttc acctaataat cttaaagtta 540

tcaagttatt aagtagagcc cattcacaag tccagatctt ttgattttaa atcctgtatt 600

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<210> 60
<211> 662
<212> DNA
<213> Homo sapiens

<400> 60
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tgagcaggat ggtcacgtac agcctggtca gtggcatctt ccgggaccca caaaggatcc 180

tgaccagcag gaccaggctg gaaccacaga gagccacaca taaaaaaatc agcccccccta 240

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cacagggctg aggattttga agatgggatg gaggatattg atgaggctta acggaaaacg 540

tataatgtgg cttctgagaa agaggaagtc ggccatggac aggttgaaga tgtagatgga 600

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cc 662

<210> 61
<211> 603
<212> DNA
<213> Homo sapiens

<400> 61
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tattattact tttattatta ttatgtactt ggttatcatt attttcattc atcaattatt 480

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ccc 603

<210> 62
<211> 427
<212> DNA
<213> Homo sapiens

<400> 62
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atacattcaa tttctggaaa tgaaaaaaaa aaattaaaaa tcttgaaagc aaacagagga 180

aaaatggcac atttcttaca gaaaaacaat aatgtaaacc acagcagatt ttccatctga 240

aaccatgaag gttggaagga aacagataat atttttgaag tactgaaaga acagaactgt 300

gaactgtaaa ttcaataccc agcaataata ttcttcaggc actaaagtga catagaaaac 360

attgtctaat gaaagaatgc taaggtaatg tgttgctaac aaacttacct ttaaagaata 420

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<210> 63
<211> 550
<212> DNA
<213> Homo sapiens

<400> 63
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<211> 1000
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<213> Homo sapiens

<400> 93
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ttgtaccttt tgcctcttca ttctgtctgc tgccttctgg gaaatgatgg gactggcagg 180

ctgtactatg cagcagggat agcagggctg tttgctctgc cctcaggaag gcagataacc 240

cctagaaaca ggaagagcca aatgaggttg tgtaagtctg aggcagaaac attagtcgtg 300

agagcaagac ttgcatttgc aagagccagg ctgtgtgtgt gtttgtgtgt gtgcgtgtgt 360

gtgtgtgcat gtgtgtgcac gtgtgtgcat gtgcgtgtgt gtgtccgtgt gtgtgtgtgt 420

aaaactggat ggccaagagc caacccctgg agggcacgga gacagggaag aaaacagagt 480

gaaacaaaaa tatttgtgta gaaggcataa aagttatcat cacagactcc actgtgtaaa 540

ggcataactt gctttattta tctctagtgt atatgaactt agcctccctt tccattcagc 600

ctgtgaaagg agatagtgct tgggccattt ggtagaagaa ggggatggga gatgatcaaa 660

accccaagta aggttcatat ccaatatagt gtctaagcag caaatgacta atggccgaag 720

aaggagacta gacagaggat tagaggcagc catggggctg gtgcagctgt ggagagctct 780

gagcaaagaa acaaggttgg caggtgagga ggcctaggat agaggccaga aggccaaacc 840

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acccctgaac aacccagatc atcttcaggg gaacagccag 1000

<210> 94
<211> 388
<212> DNA
<213> Homo sapiens

<400> 94
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tcagggttca gcaggctgta caggaagcat ggccctggca tctgcttggc ttccggtgag 180

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gagggaaagc aagagatggg ggaaggtacc aggccctttt aaacaatcac atctcacatg 300

aactcttttc tttctttctt tttttttttt tttttttgaa atggagtctt gctctgtcac 360

ccaggctaga gtgcagcggc acagtctt 388

<210> 95
<211> 662
<212> DNA
<213> Homo sapiens

<400> 95
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aaaacaaaag agaccattcc agaagtcaac aagaaaaata agtttagttt tacaagaagt 120

tcacgatctc gtccttattt taccacgtgc tagaatttgg tgaccaaagt accagaacat 180

tagtttgtag aatagtaatt tttaaactaa attttagcaa cagaacatta aaaaaaaatt 240

atctggcagc tgaatacaaa acgcaacaac aaaaaccaaa acacaaatgg agctactcta 300

gttagagtca gagaggcaga tctctgaacc atgcctgcct gcacacaact caaaaaacta 360

gtaatgtaga gtgatttctc aagcctcttc tggtatgcta aacattacag attcttctga 420

ctaaaaagag aggcaatccc tgagactctc catagaaacc ccaggctctg tagaagccat 480

gaacatttgg tattgagggt ggaggcaaca gagtctccag ctgtagtttt gttttgaacg 540

aatctggaaa ataaactgaa aaacaattta aaacaaaaag acttttaaat agtaaatgta 600

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tg 662

<210> 96
<211> 644
<212> DNA
<213> Homo sapiens

<400> 96
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gtcagggcat tgcaaaaacc tctgtgaaac ataacttttc tacattacaa aaaaatgtcc 240

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agggaataat aatagaaggc agccatccag gtatgtgggc acctgccatg ctgcagaata 480

gcagagcctc ccaagggtct aagtgccttc aaagtaaaga caactcctaa gaaagacagt 540

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ggagttccta gccctattat tgatgggcaa ctgctattga ttac 644

<210> 97
<211> 582
<212> DNA
<213> Homo sapiens

<400> 97
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taggaacaat atcacggcgg gggtgggggt tgtgtacagc ctctgcaata ttgggagtaa 120

tatcatcctt tctccccact ggatattagg aacaatatca caggaggtct ggacaccccc 180

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tggggtgtac accccttccg acattaggag taatatcatc ctctcccaca gtggatatta 300

ggaacaatat ctcagaagga gtgtagaacc cctgcggtat taggagtaat atcatcctct 360

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agtaatataa tcctctcccc atctgaatat taggaacaat atcagggggg tggggtacac 480

catttgcgat agtgggagga atatcatcct ctccccacct ggatattagg aacaatatca 540

caagtggagt atacaccccc tgcgatattg ggagtaatat ct 582

<210> 98
<211> 502
<212> DNA
<213> Homo sapiens

<400> 98
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gatctgtctg atgtaggagt ggaaagtggg tggttctttt cttccccatc ataaaggctc 180

acagctgata cccctataaa gaaagactgg ttaacaagag aaaagcacaa caaatttatg 240

aatgtgaata agtatgagag ccatacaaaa atatgaaaat tcaaagaaat ggttagacga 300

ttgatgctta actaccttct tcattaggga gaggaaagtt ggggcgggag tgggggagtg 360

gggaatgggg ccccctccat ctccaggagt ggataatggt ttgtaaataa ttctgtttgg 420

acactgaatg gagcggaatg gaaaggacaa acaataggaa tgtgaggggt ggaactgcat 480

ggtgaacaaa ggttgtctta tt 502

<210> 99
<211> 541
<212> DNA
<213> Homo sapiens

<400> 99
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ggaatgttgc cttttcctaa accacccatg gtcccgccct acaccatcct gtacctatac 120

aaaccccata ctcagccagt agacaggact atggttggac attggagaga agcagcttga 180

tggcttaaca ccgaagaaaa atccagccag agacggccag aacttccggg gagggttacg 240

ctaccgaccc tgtctccttc tcagctcccc ttcctgccga gagccacgtt tcattcacaa 300

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gtggacaaga gcgcgggagc cacaggtgga gatacaaaaa gctgtcacat tggccctttg 420

cccttgctgg cggagggcag ccgcctcaca cagaggcaga gggcccactg aactgttaac 480

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<210> 100
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<212> DNA
<213> Homo sapiens

<400> 100
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ctgttttgaa aacaattcct agactttgcc cctgttgaag ctgattgaat gctcaaccac 180

aagactccac tgttgttagc tctcgcttac tgctttttagg ggcggagtta acacttttca 240

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gctatgttga taagagatcc ctgggagctg gtaatatatt atcttctgta atttcttcca 420

aaaatagact taatggaaag aggatgcata atatacccc tctcaaagga agcgttcccc 480

aatacaacag aagcagtcat tctaaaaaca gctttatggc tctgcagtca ataactctat 540

tttctcccct ttcacaactt ccttccttct gctatgtaag aacttatgtg agggcacaca 600

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<210> 101
<211> 524
<212> DNA
<213> Homo sapiens

<400> 101
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ccagggtttg aactcaagta gcctaactat agaacccata tttttaatca ctatacagta 180

ttttactatc tgttccatca aaagaaatca tttttcagag tggagatgat agaacataca 240

tgagaacaag agtatttaaa tccaagatac ctgcaaagca tctagacact ctagatttag 300

acttttagct ccttggccaa gattaattac ctttcaggaa aataaaacta cataccaatg 360

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taatgggcta gagtcagata aatggtttct caatagattt ccagaataat ggggaaattt 480

ggttttgcat taacaatagg ctacgtatgt tatattcatt ctag 524

<210> 102
<211> 677
<212> DNA
<213> Homo sapiens

<400> 102
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tataagaaat accactacac atatctgagt ttatctttta actgtctttt agagcccatt 180

ctcttctgcc ttcctagaac ctctactatg gattatccct ttaccatagc attgtcattc 240

tcttcctttt aatgcatttg tttcccactg atttttaaac atgattgagt cattttcatt 300

agagactaaa taaacatcct cattacatgg ttcactagga ccactccctc ttcagttgtg 360

tggagaacta agcttttaga aagagacgtc caaactcagt atctctattt ctgcatgcca 420

cacaaatcca gtttgatttt catcctcatc agtctactaa aagatgtcac taaggacacc 480

aatgaattcc aaaaaagccc ctgaaatcca atggaaattt gacatttttg accactttct 540

ctttcttcaa acattcttcc cttagttttc caagatagtt ttcttctttc ctttctactc 600

actctatttt gatcttcttt gaaaattcat ccacctctac ccagtcataa aatgttaaga 660

gttgaggggg gcagtcc 677

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<211> 428
<212> DNA
<213> Homo sapiens

<400> 103
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tgaagcacag acatgacagt tgagcatgta agagatccat tgggtgctac ttgagaaagc 120

agttggactg cattctggtt ctctctgaag tttgctttta ggcaagtacc agatggattg 180

tattttagaa aagatttgtc tggaacattt cctgatgtca ttatccagag acaatgagac 240

aactcatttg cttatgaggt ttttactaca gcaatctaga gatggaattt ccaatggaaa 300

taaaaaaggg tttttataat ttctatattg acactggcag ctccgccttt taaaaaatta 360

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tgtttaga 428

<210> 104
<211> 657
<212> DNA
<213> Homo sapiens

<400> 104
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atttccaaaa gcagctgcat aatcggggaa atcagaagca tttgctaaat agtctagtgg 180

ctcattcatg gttgtctcct ttcatcttgc aagaaaacaa gagagttcag tttggcaata 240

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taaaatgagg gattgggaga aaaaagccac atgtcgcttt ggaaaacaat ttggcaaggt 540

caccatttgg agaagccata gggtatcgcc attagagact taacaacagg acctactatt 600

aaccaagtgt gatgcatgcc accatcactt acttctacat gtcacaaaat actgaaa 657

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<211> 533
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<213> Homo sapiens

<400> 105
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aaaataagag aaggaaagta aaatatagcc acaagcaaaa gtggtaacaa aatgcttgat 180

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caagtaattg gagagaagca caactatttg tggaactaag ataaaaatga attgcctcta 360

gtcagttttt gaagagccac ttgtccaggg tctcacagct gctcggccag aatttgaacc 420

ccaaccacat agttccagag cccacattct cagacatagc ccccaatact gcctctgggc 480

tggagctggt attctcaata actgtttgtt gagtggatag gtgaatcacc att 533

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<211> 595
<212> DNA
<213> Homo sapiens

<400> 106
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tcacagtggg aaggattatt actcgatcat ctgtataagc atggcccaag gagcctttgc 180

caacctactg gggatgtcac atgtaaaaag gtttctccaa aaggttggca atatgattta 240

ttaaaggagt cagatgacat gggagttaag ggcagcaaac ttcattgtga tggaaaggat 300

ctaagctgct ccagcaaaat gaaaggatta tggttcacct gccaacactg tgcaatttat 360

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ggagacatag gaaaggaaag gcagacagac cgtggaaaac agatatttcc cctggataag 480

agtggaatgg ccagtctcat aacactcatg tattatagaa ttaaatataa acctgtttca 540

gaaagtacaa tattaagacc ctttttaaat cttgatattc tttgatgata tctct 595

<210> 107
<211> 596
<212> DNA
<213> Homo sapiens

<400> 107
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aagtgagaaa gtgctattgg catctggtag attcaagcca gggatgatgc caaagatttg 240

acaaaacaca gaacaggcca tacaacagag aattatctgg tccaaaatgt caatggtgcc 300

atggttgaca aaacctgaga taagcttagg gaaggatcca gcacagagca gaatgtattc 360

tctctgtaaa gaagccaatc ccaaagagaa agaagttgag taatgctgcg tatatttact 420

cactttctct ttccaaattt cttagtttga taattcactc gacttgccct ggtaaggaat 480

gagggaggaa gcaaaaaaga ccaagcttgt gttacactaa ttactgtccc tcaacagaaa 540

aacgtgaggt gaggggtaag aaagtccccc cattctcaca tctatatcca atacat 596

<210> 108
<211> 603
<212> DNA
<213> Homo sapiens

<400> 108
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<211> 575
<212> DNA
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<400> 109
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agggtgtaat taaacagtca accacaacct gaagccactt tccctgctaa gtggacctca 300

actcaatggt ctcattctga aagatgtggc ctaaattctt gcttggaatg gtaattcctc 360

tctaatagac tctgctgttc tcttgccagt caagaggact gaaggggatt gaaggtctga 420

acctaggctc agtggctact gcccctcctc cacagccgct ggcttccagc agacattcct 480

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<210> 110
<211> 402
<212> DNA
<213> Homo sapiens

<400> 110
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gacaaccctg cctgacacca ggcctagtgt ggctccatga taacaaagac gcaggtccag 360

agacaatccc cctacatggt gcctgcatct gattcccctt gg 402

<210> 111
<211> 564
<212> DNA
<213> Homo sapiens

<400> 111
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ggctccctgg gctacagagg tctggagaga agctggcacc tgggaagaac aatttcccca 180

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actcatcttc cttgtccttt gcttcatgac accttgagcg tgttagaagc taatcctgaa 360

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gcttgagagt atgcatccaa tgcagctagg tcctccacac actgtggtgg ggcccctcac 540

cctcagatca gcatcttact ctca 564

<210> 112
<211> 433
<212> DNA
<213> Homo sapiens

<400> 112
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atctgtcctg acaaaacatg tctcaatttc tttctaaagc agctctattg tcctagcata 180

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gtaggttagg ttccaaaacc acccttccta gccctccctg tagaaaatac catgttgcac 300

agttacatgt gtcccctgac acaaacgaca ctcattttac gtaggtcact ggacctcaaa 360

ctgttgttgc ttgctgtccc agccaattca agagtgaagg aagatgtaac cagacataca 420

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<210> 113
<211> 461
<212> DNA
<213> Homo sapiens

<400> 113
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gtttgggcta ctatttcatt ttaccatttt atccctatta gtatttatca ccatacattc 180

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ttccaatctc tgataaagtg ttgaaagggt accattatgc ctctcagaga tacacacagt 420

catgtgccac ctaactatgt ttcagtcagt gagggaccat a 461

<210> 114
<211> 444
<212> DNA
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<400> 114
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gtttgcatcc ttgcatctgt gtgt 444

<210> 115
<211> 473
<212> DNA
<213> Homo sapiens

<400> 115
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ccaagactcc acaaaggcat aggggctttg tgggagaatg gcagtcctcc tggagaagtg 180

gcagataaaa aggtaaagat ctgtgagcaa cgtcatcttg agttcaggaa ttgacaatag 240

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gagattttaa tctccttaat agaaagttgt ttgtattgat tgaatgatta acctttatta 360

agaattttgt tgtctcaggc actggattag tagctttaca catttcattt aaatctcaca 420

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<211> 261
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<213> Homo sapiens

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aaagttttaa caaaatctca cggtaactct tcagaagcaa aaataaaata ataacattta 180

ataaaagtgc ctgctcaagg cctgcagccc aattccaggt ttgctccaaa tgttgatggc 240

cttgagcttt cttgtgtgaa a 261

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<213> Homo sapiens

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atgggttgca ggagcaccat gaggttcatc taatctttgc cttcctctgc cagcatgtgt 120

gccatctgca atgtctcact gagcactgag tggggcctgc tatgtgggca gtatccctgc 180

catcttcata tca 193

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<212> DNA
<213> Homo sapiens

<400> 118
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ctcatgtatg ttctatcatc tccactctga aaaatgattt cttttgatgg aacagatagg 180

aaaatactgt atagtgatta aaaatatggg ttctatagtt aggctacttg agttcaaacc 240

ctggctctga cgctttctaa ctgtgtgact gtggacacga tatacaacct ctattaattt 300

caatattacc atttgtgaga aaaggaatga taacaatatc catatcatgg tgggttcttt 360

tttt 364

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<211> 425

<212> DNA
<213> Homo sapiens

<400> 119
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gatatcaaat aagcagatct acacaaagga atgaagatct tcagaaatcg taaaattgtg 240
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agaaaaatgc tagcaatttg ttatgaggtt taaaatatgc agaagcagaa gtaaatcata 360
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cattctgaag gctcttatgt acatgcatta aacaaatttg tatctcctat taatgtgcct 360
tttgcgagtt gatttttcag tgaaacttca gaggtccaac ggcagtagcc cctaccaagt 420
tcaagatgct ccacttac 438

<210> 121
<211> 482
<212> DNA
<213> Homo sapiens

<400> 121
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gcttatccat tctttcttgt ttacagaaag acttaatttt ctgtctcata tctctgtcct 180
tcttgcccca ctatttttcc cccttctcca aaaatcccag ccccaaaaac agtctacata 240
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tcacacacac aaaatattgg atatgagtga gattttaaaa aattggtttt taaatgtgat 360
gaaaagagtg tccttttcac cagaacaaaa caaccettaa tgctgaagcc tccttcccga 420
tatgggtggc ttccaaatat gaagaaatct gtgcattggg ccacaggctc cagacaaagt 480

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<211> 568
<212> DNA
<213> Homo sapiens

<400> 122
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acctcacaca gcctgagtgg gcctgagata ggctgagggg cctaagcttc aattgcataa 120

gcagggctag gtcactccag ttaccaaaga cagaaacaga tagtccagag ccgtccaggg 180

gatgctagcc actgcccagg agatgatcag agaacacaca acagaaatca gaaaatgtag 240

tacaagaaga atttgctgat aggtgcaatc gcctcagcaa ggcacaggaa actcaactca 300

gaaggcagtc tgtctgtcat ccaccaattc tctgggtcaa gtctgatgtg cactcataaa 360

gtaaaaatgc actgttattg tgactgagaa aaaaaataaa gctaaaaggt aagtgcctat 420

aaaataagat tttactaatg caaacaaaag ccctaaagaa gtgtggtttg agcccagtgt 480

cctcctctat tagcaccaac aatggatagg tggttgagtc tgtcaaaatg cctctgggtt 540

tacagaaatg aaagcttggt ctgtgccc 568

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<211> 413
<212> DNA
<213> Homo sapiens

<400> 123
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gctaaattta aatgagaaaa agagcttgtt gcacttgttg atccagttgg atccagtttt 180

ctctgctggt ccatttttg tatccctttt gagtttgcat tcctttttaa catttttgg 240

tatagcagat ttttattttt tggtacattt gtgcacataa acttcttggt gtggaggaga 300

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<210> 124
<211> 525
<212> DNA
<213> Homo sapiens

<400> 124
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cttaggtttc ttctctactt cccttttaa ttgaagagtt taatgcatgt atctgtgtgt 120

ttgcttgaaa aaaaacacca agtataacat gttctatcta tgaatacttc tggccattaa 180

ctcaaaaggt actatattac agacagaaaa gcaccagaaa gcaatcaggg acttcatcta 240

agaggtagga cagcatagtt ggtaaaaata cagaccctgg aggcaaactg cctgggcttg 300
aatcccagct ttattacttt gggaaaacta cttatcttct ttacttgttt tggtatccat 360
gtctgtgaaa tggaagtaat aataatcctc tcatagcatt gttgtgaggt ttcaatagat 420
gaagtgaaga ctttagaagg gcacatgata agaattatat aagggttacc tattattgct 480
atccaatttg tcatagcaag ctaagggacc ttgggcaagt tactc 525

<210> 125
<211> 575
<212> DNA
<213> Homo sapiens

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taagcattta gtctcatcac aaattctgtt ttagaaaaaa acaacagaaa atagtgaatg 180
agaagggtag gagacttagg actcagcgaa ttctatctca gtgccaagac tttaaaactg 240
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ctagagggtg gtgtggtaca gtgggaggaa tggactttgg agtgagatcc atgttcaaat 360
cccaagtcac ttaccttctc tgatcctcag tttcctcatc tgtaaaatga ccataatcaa 420
caccatctcg aagatttgtg gtgacaacac agcatttact tcctgctgta tacttcccat 480
ttcctcttgt agagacagaa ttttccactt tattttaatc tataattatg taatcccatt 540
taaaaatcac ccttcgactt tcagttccac aaggc 575

<210> 126
<211> 638
<212> DNA
<213> Homo sapiens

<400> 126
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taatctggac ttggaattcc atcatacaga ggccaagtct ctgaccatga tgttctctct 180
gtgtaactgg ggctgctgaa acccaagtat tgtcagccag tgccggtctc cagccatgct 240
tgtgtctttt aagaagtgac agtaactgct atttgtggag atggctattc atagggactc 300
cttttctttg cctgacagag gcccagtgtt ctaagctcta agaggggctc tgatgccagc 360
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acatcactac ctcctctccc cctgcccagc ttgcattgtc gcccttcccc atctaccatg 480
ctgtccttga acataaggcg cttctctgca ttccatgtgt ctactttgta gttatgtgct 540
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caatagatgg gtttaatata tcttatgatt ggttcttg 638

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<211> 573
<212> DNA
<213> Homo sapiens

<400> 127
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cggtattctg gctaccatag ctatcttgct ctttttgttt ataattatga tatgttccaa 180

aaaggagtaa aacgtaatac aagaagataa aaatacattt accattaagt aagaaaaaag 240

acaagggaga agagaataag aaaatgagtc aggagtggga tttatacaaa aaattagtga 300

gtccacttta cttcctggaa gtggatggtg agcttttctt gccagccttc ttgaagaggg 360

aagcactgtc agttatgttg tagtgtgtcg atctagtaaa atccaactgg ttgttcagat 420

acctagatga atattcttga taggaagatg aaaaaaaaat ttcttccaaa gtcttcatgg 480

atacataaag tgtataatga gcaaaacctt tgacatgttt acagtaaacc caatggtgtg 540

tttcacctgg cctttctctt ctttcgttta ctg 573

<210> 128
<211> 461
<212> DNA
<213> Homo sapiens

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cgcatgtaat tgtcaagcgt ggcagggcag tattgctctc aaagtcccgt ctgactgaca 120

gggcagaggt tcttcctcac tgcccgaatc tgcttcccga cagctccagg gttccctcag 180

gaagccgccc tccaccttca cctcaggcat gtcctgcaga gccctctgga gaaccagctt 240

caggttctgc ctattttgac gctgcctaaa ggagcccacg aagaagtaaa tgacggggtt 300

ggcactaccg tttagaggag acaggaaaat ggaaactaga tggacatgac agaaaatgac 360

ttccaaatcc aggtgtatcc cagtagacag agcccaccga atgccgaagg gcaggctgcg 420

gagtaggaag actagcactg tgagcaggat cgtcacgtac a 461

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<211> 655
<212> DNA
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ggtagaccaa ctctgtgatg gagttatgag atggggaagg agggtctggc accatgcaac 120

aggatttccc ccaaagctca gcactccaag gagcacatca gcatcaggaa tgtctgctgg 180

aagccagcgg ctgtggagga ggggcagtag ccactgagcc taggttcaga gcttcaatcc 240

ccttcagtcc tcttgactgg caagagaaca gcagagtcta ttagagagga attaccattc 300

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caccattgta tgcaaagtac agcatctctg acaagcaagg aacactggct tgccccacag 480

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actacctcta gcaggggcat gacattcccc aagagagggc atctccttta gcctggacct 600

tggagcaaaa gcaacccatg gatcagacca atagacaaca tgcagccctc atcta 655

<210> 130
<211> 657
<212> DNA
<213> Homo sapiens

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ggaaatgagg acacagtggt gtcattgggt tttgattgtc cacttggaaa aggttaaaac 180

ctgtcctaca gtcatgatga cttcagttcc atttaagtgg ggtcctgtct ctctcactct 240

ccaccgactg tacctttact ataacatggc cttatataga tagctttgag taagtgtgtg 300

ttaaatgact gcccaagtga atggaaaatt gagaagggcc tccagcactg gagtatggaa 360

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aaggacatgg atcttgacag tgttggaatc ttcagaaata attgcaatac cagaagttat 480

ttaagatttt accattttca aagtatttgt acgtaacact ttcatatgtt tttgtttcct 540

agctacctca gtttccctgt tggcttgagc agattagtgt aaagaggtgg tgacatcagg 600

ggaaacaggt ttactcagcc atcttcatta ccatattatc actgacttga ggctcct 657

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<212> DNA
<213> Homo sapiens

<400> 131
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actactgctg tctggctcca ctcgagggaa gccaggtaac ctgtgttagg ccgcgctttt 180

cctggcggcc ttgtaaatct gttagtacat gaaaagcatg acgcacatgg ggattaggat 240

gccaatgcgg tggagtaaat cgtgtagcca aagtcttgac tgaccaagca caccttatca 300

tcgtttacat tctgagcccg accaaaaatg gtaggtaaag tgacaaaggc ggaaagaagg 360

cagacagaaa gaatcatctt cgtcatgcat ttccccttct gcctcatagg gtacgtgaga 420

ggcttcatga tcccaaggta cctgtcgatg ctgatcacgt acaaggtcaa gatccaggcc 480

gtgcagcaca tgacattcac ggagaagacg ttacagaaaa agtgtccaaa gatccacttg 540

cccccgatga ggtcggtgac actgat 566

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<211> 575
<212> DNA
<213> Homo sapiens

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agtctttagt ttaaaaaaca acaaaaaact gtatacacat atatatataa aatcaggtag 180

tataaagaaa aacagaactc cagagattcc tgggtcacag aaggggaaag ggctgttcaa 240

gaaagtgaaa ttgaactaac tgaaaataca gctatcttta tattggaagg acagtcagga 300

agtcaacaga taaggcctaa actgcataaa gcaggaaaca gcagactaaa gacattatta 360

agaaatatgg aacacaacca aaagaaatag caaaaacaat gaaaagtgac tgtttttcat 420

aagtgaggca ggggaagaga aggggttatt tttttcccca ttatatgtct ttaagaacta 480

cttgctaaaa atattgggca catatgaatt tgataaaagc gaaaaacttt ttacttcaca 540

agtgcagctt taacatacgt tgattacagt gaagt 575

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<211> 651
<212> DNA
<213> Homo sapiens

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tgcatgagga aaagtctgaa gaaaccaggg acagcttcca agattctttt cccagtgaaa 240

ttacacagga tatgcttaat tctttcagca aggaattgtg acaagacatg tgaaacacta 300

cctgccaggg aagttcctta gtgactcagt gcccatggtt attattgggg actggtcacg 360

tatgccctct ttgcctcata cttagagaat tccagttcca gaaggaaagc aggtattcag 420

tataagccat attatttgca tagaccagtt taggatcaag gaattgtagg aagcttttca 480

aaatctaaga ccccaaatac cagccaagag ccagccttgc aagcaggaca ttttaagagt 540

agcagtcttg ggtctgctgt attaactctt ttctgcacag aaatgatagt atgacatcta 600

agttattatt atcaagggac cgagaaatgc atgtttttta ggctagggaa g 651

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<211> 966
<212> DNA
<213> Homo sapiens

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ctctttgtct gggtgcggag gagctcccag cagtggcggc ggcagcccac acggctgttc 660

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<210> 135
<211> 198
<212> PRT
<213> Homo sapiens

<400> 135

Lys Lys Gln Val Ser Leu Thr Glu Gln Glu Thr Ile Leu His Phe Phe
1 5 10 15

Lys Trp Gly Lys Thr Glu Gln Leu His Glu Lys Tyr Asn Ser Leu Tyr
20 25 30

Ile Lys Leu Ile Gly His Glu Leu Ala Leu Gln Val Glu His Asn Asn
35 40 45

Ser Arg Ser Lys Ser Arg Leu Pro Ser Lys Ser Cys Ser Ile Arg Arg
50 55 60

Phe Phe Ile Gln Asp Ala Lys Ile Ile Lys His Asn Asn Cys Ile Glu
65 70 75 80

Leu Asn Glu Asn Arg Gln Cys Phe Ile Ile Glu Lys Phe Ser Asp His
85 90 95

His Ala Lys Ile Phe Leu Ile Phe Asn Phe Leu Cys Arg Ile Ile Phe
100 105 110

Met Ser Met Gly Tyr Phe Glu Tyr Arg Arg Ala Met Cys Asn Asn Tyr
115 120 125

Ile Arg Val Asn Ile Val Ser Ile Thr Ser Ser Val Tyr His Leu Cys
130 135 140

Tyr Lys Gln Ser Ser Tyr Ile Leu Leu Val Ile Leu Asn Cys Thr Thr
145 150 155 160

Lys Leu Tyr Leu Gln Ser Pro Cys Cys Ala Ile Tyr Ile Leu Phe Ile
165 170 175

Phe Phe Leu Thr Ile Phe Cys Thr His Pro Ser Ser Leu Tyr Ser Pro
180 185 190

Ser Ala Gln Leu Asn Ser
195

<210> 136
<211> 214
<212> PRT
<213> Homo sapiens

<400> 136

Arg Cys Ser Ile Val Ser Ser Val Ser Cys Pro Leu Leu Pro Pro Gly
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Val Asp Ser Cys Thr Val His Pro Thr Pro Ala Phe Pro Ser Phe Leu
20 25 30

Ile Ser Pro Val Ile Phe Pro Val Ala Leu Leu Cys Trp Cys Pro Val
35 40 45

Arg Ser Cys Gly His Lys Arg Leu His Gly Pro His Pro Gln Leu Gly
50 55 60

Glu Ser Ser Pro Ser Trp Val Leu Trp Thr Val Lys Lys Asp Gly His
65 70 75 80

Val Gly Ser Val Glu His Glu Val Val Gln Asp Leu Gly Gly His Arg
85 90 95

Ser Cys Leu Pro Ala Ser Arg Ala Leu Pro Pro Phe Gly Ser Leu Leu
100 105 110

His Leu Gly Lys Arg Phe Val Pro Thr Pro Arg Arg Val Asn Arg Ala
115 120 125

Pro Trp Trp Ser Thr His Cys Pro Ser Glu Gly Pro Ser Ser Leu Met
130 135 140

Ser Trp Cys Pro Gly Leu Pro Gly Arg Ile Leu Ala Ala Leu Pro Gly
145 150 155 160

Pro Glu Met Asn His Trp Glu Glu Ile Gly Asn Glu His Thr Ala Ala
165 170 175

Thr Leu His Pro Asn Pro Val Pro Tyr His Arg Arg Leu Leu Trp Gln
180 185 190

Asp Asp Ser Ile Ser Val Cys Leu Arg Ser Leu Phe Leu Pro Arg Leu

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        195                 200                 205

Leu Pro Pro Gly Arg His
    210

<210>  137
<211>  141
<212>  PRT
<213>  Homo sapiens

<400>  137

Ile Ile Ser His Thr Ala Phe Phe Arg Phe Ser Leu Ser Ile Cys Phe
1               5                   10                  15

Cys Asn Ser Tyr Trp Thr Phe Thr Ser Leu Ser His Cys Leu Leu Tyr
            20                  25                  30

Leu Leu Thr Phe Val Phe Ser Val Ser His Cys Cys Ile Val Ser Tyr
        35                  40                  45

Tyr Leu Ala Leu Pro Val Asn Ser Leu Ser Phe Phe Cys Asn Leu Phe
    50                  55                  60

Ile Ser Ser Leu Cys Leu Leu Phe Gln Leu Asn Leu Ile Ala Gln Ser
65                  70                  75                  80

Phe Ile Trp Ser Phe Lys Ile Cys Phe Cys Leu His Ser Tyr Phe Val
                85                  90                  95

Leu Phe Ser Leu Ser Leu Tyr Leu Phe Leu Met Leu Ser Ser Ala Tyr
            100                 105                 110

Tyr Phe Asp Ile Tyr Phe Leu Ala Ser Leu Arg Tyr Ser Ile Ile Ser
        115                 120                 125

Gly Pro Arg Ile Ile Lys Ser Pro Thr Thr Ser Val Asp
    130                 135                 140

<210>  138
<211>  223
<212>  PRT
<213>  Homo sapiens

<400>  138

His Glu Trp Leu Thr Phe Phe Ile Glu Asp Glu Ile Leu Ser Trp Cys
1               5                   10                  15

Ile Tyr Val Pro Cys Tyr Phe Pro Ala Asn His Phe Ser Asn Thr Ala
            20                  25                  30

Gln Leu Tyr Ser Asp Thr Val Asp Thr Val Phe Gln Ala Leu Tyr Phe
        35                  40                  45

Gln Phe Ile Cys Gly Ile Leu Asp Ser Phe Gly Ser Ser Thr Glu Val
    50                  55                  60

Thr Phe Ile Tyr Arg His Phe Arg Gly Ile His Thr Thr Ser Tyr Asn
65                  70                  75                  80

Cys Thr Ala Ile Ala Cys His Cys His Val Phe Ile Asn Phe Gln Phe
                85                  90                  95

Leu Glu Asp Phe Ser Ile Ile Ile Tyr Lys Leu Val Lys Phe Thr Val
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            100                 105                 110

Ile Cys Gln His Leu Glu Gln Glu Lys Met Ser Ala Lys Asp Gly Arg
        115                 120                 125

Thr Leu Tyr Phe Ile Leu Ile Ala Gly Phe Leu Pro Asp Asp Asn Phe
    130                 135                 140

Gln Lys Ile Asn Pro Asn Phe Asn Thr Ser Cys His His Phe Thr His
145                 150                 155                 160

Ser Asn Ile Lys Ile Ser Asn Phe Thr Tyr Ile Ser Ser Glu Ser Thr
                165                 170                 175

Asp Lys Leu Phe Tyr Ile Glu Gly Asn Ile Ser Trp Glu Val His Asn
            180                 185                 190

Cys Thr Cys Arg Ile Ile His Arg Ser Phe Gln Val Leu Leu Leu Gln
        195                 200                 205

Ile Gly Leu Lys Ser Ile Thr Val Gly Leu Ser Val Ala Gln Lys
    210                 215                 220

<210>  139
<211>  173
<212>  PRT
<213>  Homo sapiens

<400>  139

Asn Ile Ile Thr Phe Phe Tyr Glu Tyr Ser Trp Ser Phe Gln Asn Lys
1               5                   10                  15

Thr Ser Tyr Trp Phe Asn Lys Leu Trp Tyr Asn Gln Ile Met Lys Leu
            20                  25                  30

Tyr Ala Phe Val Lys Val Thr Phe Gln Lys Asn Ile Leu His Arg Ile
        35                  40                  45

Thr Asp Pro Ser Ala Leu Pro Thr Leu Trp Ala Leu Ser Leu Phe His
    50                  55                  60

His His Tyr Leu His His Cys Leu Gln Val Phe Tyr Thr Ala Arg Val
65                  70                  75                  80

Gly Leu Cys Leu Leu Asn Ser Gln Val Lys Arg Gly Arg Lys Leu Thr
                85                  90                  95

Pro Ser Gly Gly Ser Leu Gly Met Ile His Gly Arg Trp Ser Ile Asn
            100                 105                 110

Thr Ser Ala Leu Phe Pro Leu Glu Ile Leu Arg Asn Gly Phe Tyr Ile
        115                 120                 125

Val Ser Gln Ser Phe Leu Lys Val Leu Asn Phe Asn His Pro Gln Gly
    130                 135                 140

Val Val Gly Phe Ile Ile Val Tyr Ile Pro Leu Trp Leu Pro Phe Leu
145                 150                 155                 160

Leu Val Ser Leu Leu His Ser Lys Leu Gly Phe Ile Ser
                165                 170

<210>  140
<211>  223
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<212>   PRT
<213>   Homo sapiens

<400>   140

Val Phe Leu Ser Arg Lys Glu Glu Lys Gly Trp Val Val Thr Gly Gly
1               5                   10                  15

Gln Gln Cys Gln Asn Trp Gly Val Trp Thr Gly Ile Gln Glu Asn Glu
            20                  25                  30

Gly Ala Gln Asp Glu Gln Lys Gly Gly Glu Ala Ile Phe Ile Lys His
        35                  40                  45

Leu Leu Cys Ala Ser Gln Ala Arg Leu Gln Ile Ile Thr Leu Leu Lys
    50                  55                  60

Ser Ser Gln Gln Pro Ser Asn Arg Tyr Leu Ser Leu Ile Pro Tyr Pro
65                  70                  75                  80

Cys Ser Ala Ser Pro Pro Ile Thr Met Ala Glu Glu Phe Lys Pro Leu
                85                  90                  95

Ser Lys Ala Ser Thr Val Ile Cys Pro Leu Asp Pro Ile Pro Ser Ile
            100                 105                 110

Phe Leu Phe Ile Glu Thr Phe Ser Met Val Phe Lys His Thr Leu Leu
        115                 120                 125

Ser Leu Leu Leu Asn Arg Gln Met Gln Leu Ile Lys Leu Phe Phe Ser
    130                 135                 140

Leu Gly Tyr Cys Pro Ile Ser Leu Leu Pro Phe Met Ala Glu Leu Leu
145                 150                 155                 160

Glu Arg Val Phe His Asn His Phe Ile Ser Thr Pro Leu Thr Asp Phe
                165                 170                 175

Thr Gln Leu Glu Glu Glu Glu Gly Thr Leu Ile Pro Lys Cys Pro Ile
            180                 185                 190

Lys Pro Asn Pro Leu Lys Val Leu Cys Cys His Asp Gly Cys Glu His
        195                 200                 205

Gly Glu Lys Ile Leu Glu Asp Val Gly Asn His Asp Arg Glu Thr
    210                 215                 220

<210>   141
<211>   176
<212>   PRT
<213>   Homo sapiens

<400>   141

Ser Cys Glu Thr Ser Ile Leu Val Ser Trp Gly Gln Gly Asn Gln Gly
1               5                   10                  15

Pro Ser Met Leu Ile Leu Pro Cys Val Arg Leu Ile Leu Ser Ile Ser
            20                  25                  30

Gly Gly Gln Val Ala Thr Trp Pro Pro Gly His Thr His Gln Glu Phe
        35                  40                  45

Ile Leu Cys Asn Leu Glu Glu Gly Leu Arg Asn Ala Gly Gly Tyr Leu
    50                  55                  60
```

Pro Gly Asp Ile Leu Tyr Pro Leu Ile Gly Asn Trp Gly Arg Ser Gln
65 70 75 80

Phe Gly His Thr Phe Pro Glu Leu Asn Phe Tyr Glu Gly Asp Leu Gly
85 90 95

Gly Arg Gly Ser Glu Ala Asn Ile Ala His Val Pro Gln Thr Leu Val
100 105 110

Cys Leu Thr Glu Ile Tyr Ile Phe Ser Asp Lys Phe Phe Lys Ser Leu
115 120 125

Leu Tyr Val Phe Arg Thr Ile Ser Gly Asp Phe Leu Lys Asn Asn Phe
130 135 140

Cys Leu Leu Tyr Leu Phe Ser Ala Val Thr Gly Pro Gln Ser Pro Tyr
145 150 155 160

Asn Val Asn Pro Glu Val Glu Leu Leu His Tyr Ser Phe Phe Phe Phe
165 170 175

<210> 142
<211> 209
<212> PRT
<213> Homo sapiens

<400> 142

Ser Gln Lys Asn Thr Thr Pro Leu Leu Glu His Asn Val Ile His Phe
1 5 10 15

His Leu Leu Ala Ser Leu Ala Glu Phe Gln Lys Cys Asn His Tyr Glu
20 25 30

Ala Gly Thr Lys Asp Phe Pro Asn His Phe Val Ile Leu Ile Asn Ile
35 40 45

Ser Ser Ile Leu Leu Asp Pro Phe Thr His Phe Leu Tyr Cys Phe Pro
50 55 60

Phe Pro Glu Val Leu Asn Lys Ile Ser Leu Leu Phe Val Leu Glu Lys
65 70 75 80

Ser Ser Cys Leu Pro His Arg Met Val Val Gly Glu Thr Gln Trp Glu
85 90 95

Thr Ser Val Lys Gly Gln Lys Thr Leu Thr Phe Val Ile Val Ser Ser
100 105 110

Phe Phe Gln Asn Thr Ser Ile Ala Trp Leu Leu Tyr Thr Arg Leu Leu
115 120 125

Lys Ile Tyr Leu Cys Pro Thr Thr Leu Phe Val Val Asn Ile Phe Leu
130 135 140

Ile Leu Ile Gln Tyr Ile Ser Glu Ile Phe Asp Leu Gln Ser Asn Leu
145 150 155 160

Ser Ile Thr Met Ile Pro Tyr Leu Asn Thr Gly Met Val Lys Met Arg
165 170 175

Thr Asn Leu Pro Phe Leu Cys Ser Tyr Arg Gln Ala Ile Leu Ile Thr
180 185 190

```
Asn Val Gln Ser Lys Pro Met His Glu Cys Arg Met Gln Leu Lys Ser
        195                 200                 205

Arg


<210>  143
<211>  200
<212>  PRT
<213>  Homo sapiens

<400>  143

Ser Phe Pro Val Ser Glu Lys Ile Lys Pro Cys His Ser Lys His Val
1               5                   10                  15

Leu Pro Lys Phe Lys Lys His Val Asn Leu Leu Val Lys Leu Tyr Val
            20                  25                  30

Leu Val Asp Phe Glu Ile Leu Cys Asn His Leu Lys Leu Ala Ser Gly
        35                  40                  45

Pro Gln Leu Asp Gln Ile Pro Val Ser Leu Phe Leu Thr Ser Leu Cys
    50                  55                  60

Trp Thr Thr Tyr Leu Gln Arg Gln Lys Lys Asp Lys Ser Asn Asn Pro
65                  70                  75                  80

Thr Val Ile Leu His Lys Ser Met Thr Lys Leu Pro Leu Gln Lys Leu
                85                  90                  95

Asn Ser Ser Ser Leu Asn Phe Leu Thr Ile Thr Trp Lys Ser Ala Thr
            100                 105                 110

Met Val Asn Cys Gln Thr Cys Thr Ala Ser Gln Pro Thr Leu Tyr Thr
        115                 120                 125

Asn Lys Gly Gly Leu Tyr Ser Asp His Tyr Trp Asn Lys Leu Ser Leu
    130                 135                 140

Pro Asn Val Ser Ser His Pro Leu Asn Tyr Leu Leu Leu Leu Tyr Phe
145                 150                 155                 160

Tyr Thr Ala Ile Lys Leu Lys Leu Leu Lys His Asn Phe Ala His Val
                165                 170                 175

Gln Asn Phe Tyr Ser Val Pro Gln Gln Ser Leu Thr Asn Pro Gln Asn
            180                 185                 190

Leu Pro Thr Asn Leu Phe Leu Thr
        195                 200

<210>  144
<211>  170
<212>  PRT
<213>  Homo sapiens

<400>  144

Val Ile Pro Ser Ser Val Cys Pro Thr Val Gly Leu Pro Asp Thr Asp
1               5                   10                  15

Ser Thr Thr Leu Val Ile Cys Asp Phe Leu Phe Thr Gly His Glu Lys
            20                  25                  30
```

Pro Phe Thr Asp Trp Leu Gln Cys Ala Ser Leu Pro Tyr Gln Leu Leu
35 40 45

Phe His Thr Asn Ser His Leu Val Asn Trp Val Pro Cys Ser Ala Lys
50 55 60

Met Cys Phe Ser Ala Gln Val Ile Leu Tyr Thr Pro Ile Leu Asn Leu
65 70 75 80

Leu Cys Ala Ser Gln Ser Thr Ile Phe Gln Ser Gln Leu Lys Pro Phe
85 90 95

Ile Ile Gln Tyr Gly Phe Ser Pro Gln Ser His Val Lys Val Ser Pro
100 105 110

Cys Phe Phe Gln Thr Val Val Ala Leu Thr Gly Leu Leu Leu Gly Tyr
115 120 125

Lys Leu Thr Leu Tyr Phe Ser Ile Phe Ser Leu Pro Trp Ser Lys Arg
130 135 140

Lys Ile Arg Ser Met Asn Leu Arg Thr Tyr Lys Leu Leu Val Glu Gln
145 150 155 160

Gly Leu Asp Ile Val Cys Ile Asp Ser Arg
165 170

<210> 145
<211> 214
<212> PRT
<213> Homo sapiens

<400> 145

Met Gly Thr Ala Leu Phe Lys Val His Phe Pro Asp Ser Ala Val Leu
1 5 10 15

Phe Ser Ser Ser Ile Pro Thr Asn Ser Gly Leu Gln Ala Phe Pro Leu
20 25 30

Leu Ser His Ser Ile Leu Pro Glu Pro Ser Ile Lys Ala Pro Thr Ile
35 40 45

Leu Pro Ser Gly Gly Ala Ile Phe Leu Ser Phe Pro Glu Arg Trp Asp
50 55 60

Pro Leu His Phe Thr His Leu Ser Pro Arg Pro Ser Thr Cys Leu Ala
65 70 75 80

Gln His Ser Asn Ile Asn Pro Val Glu Ile Asn Cys Gly Ile Ala Trp
85 90 95

Phe Pro Trp Met Val Ile Gln Val Val His Cys Thr Thr Met Cys Asn
100 105 110

Ile Pro Gly Lys Arg Gln Lys Phe Ile Asp Trp Leu Gly Val Leu Asn
115 120 125

Ser Gln Gly Lys Leu Phe Asp His Cys Met Pro Ser Thr Trp Glu Asn
130 135 140

His Ile Pro Gln Leu Leu Arg Pro Tyr Cys Met Val Thr Trp Gly Asn
145 150 155 160

Ile His Thr Val Ser Pro Ala Leu Ser Ala His Lys Gly Asp Ile Val

165 170 175

Gln Arg Gly Asn Leu Ser Leu Pro Ser Thr Ser Leu Phe Leu Thr Pro
180 185 190

Lys Ser Leu Ser Leu Leu Thr Lys Asp Ile Ser Ala Ser Ala Ile Leu
195 200 205

Phe Ala Glu Trp Arg Ile
210

<210> 146
<211> 200
<212> PRT
<213> Homo sapiens

<400> 146

Arg Ile Ser Gln Lys Cys Cys Val Leu Leu His Pro Leu Trp Gln Leu
1 5 10 15

Phe Val Tyr Leu Ser His Ala Gly Glu Val Asn Thr Asp Pro Leu Val
20 25 30

Lys Met Met Ser Asp Ile Phe Phe Ser Ala Ala Asn Leu Ser Ile Phe
35 40 45

Ser Phe Val Ile Met Gly Ile Leu Trp Lys Val Thr Trp Arg Leu Cys
50 55 60

Lys Ile Tyr Ser Ser Gln Phe Tyr Leu Pro Val Leu Ala Ser Ile Asp
65 70 75 80

Val Ser Cys Leu Ser Leu Leu Ala Gln Phe Ala Lys Cys His Tyr Leu
85 90 95

Pro Phe Ser Ser Met Arg Cys Met Tyr Val Tyr Met Tyr Ile Cys Ile
100 105 110

Asp Ile Ser Val Tyr Leu Glu Thr Tyr Ile Asp Glu Leu Ser Ile Thr
115 120 125

Met Ile Ile Tyr Phe Asp Val Gln Val Val Pro Asp Leu Thr Ser Asp
130 135 140

Ser Phe Leu Asn Leu Met Tyr Gln Asp Val His Lys His Val Phe Phe
145 150 155 160

Pro Cys Pro Asn His Pro Gly Val Gly His Leu Ser Lys Met Ser Cys
165 170 175

Phe Cys Leu Leu Arg Trp Arg Ser Gly Ile Gln Lys Ser Arg Ser Val
180 185 190

Cys Leu Val Cys Phe Ile Ala Ile
195 200

<210> 147
<211> 191
<212> PRT
<213> Homo sapiens

<400> 147

Tyr Leu Ile Leu Lys Tyr Ile Ile Met Lys Ser Ile Asn Val Ser Arg

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1               5                   10                  15

Gln Arg Ser Tyr Ile Pro Lys Ile Gly Asn Asn Cys Val His Met Cys
            20                  25                  30

Tyr His Thr Ile His Pro Ile Leu Leu Tyr Leu Asn Phe Pro Lys Gln
        35                  40                  45

Pro Val Val Lys Gln Leu Val Met Arg Thr Asn Glu Lys Leu Pro Glu
    50                  55                  60

Ile Ser Asp Ser Ser Cys Thr Tyr Phe Thr Pro Glu Val Trp Glu Phe
65                  70                  75                  80

Thr Glu His Asn Val Arg Phe Phe Ser Ile Ser Tyr Pro Leu Pro Lys
                85                  90                  95

Ile Val His Lys Ile Gln Asn Ile Ser Ser Leu Thr Phe Leu Glu Cys
            100                 105                 110

Asn His Thr Leu Asp Asn Tyr Phe Arg Leu Leu Asn Gly Lys Arg Thr
        115                 120                 125

Gly Arg Arg Val Lys Val Thr Cys Phe His Leu Ser Tyr Phe Arg Leu
    130                 135                 140

Thr Ser Lys Ser Phe Phe Thr Leu Phe Leu Ile Leu His Arg Pro Phe
145                 150                 155                 160

Leu Val Lys Ser Ala Asp Ser Lys Tyr Lys Ala Asn Ala Tyr Ser Tyr
                165                 170                 175

Val Ile Phe Met Phe Phe Lys Asn Asn Met Val Leu Thr Ser Ser
            180                 185                 190

<210>  148
<211>  193
<212>  PRT
<213>  Homo sapiens

<400>  148

Gly Leu Ser Glu Gly Glu Ala Ser Leu His Leu Asp Phe Phe Leu Lys
1               5                   10                  15

Ile Thr Thr Ile Met Asn Thr Ala Ala Thr Ser Leu Leu Cys Thr Arg
            20                  25                  30

Gly Ile Ile Leu Gly Val Ser Val Tyr Ala Tyr Pro Glu Ile Ser Ser
        35                  40                  45

Phe Leu Leu Arg Gly Glu Val Leu His Ile Asp Phe Ile Val Arg Asn
    50                  55                  60

Gly Lys Ile Phe Asn Lys Cys Ile Arg Ala Thr Thr Phe Ser Ala Leu
65                  70                  75                  80

Gln Pro Ala Ser Pro Pro Ser Arg Gln Asp Ile Met Asn Pro Leu Phe
                85                  90                  95

Gly Lys Ala Ala Glu Lys His Val Leu Gln Thr Tyr Tyr His Leu Val
            100                 105                 110

Asn Asn Ser Gln Trp Thr Asp Gln Asn Ser Arg Arg Phe Pro Leu Ser
        115                 120                 125
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Leu His Cys Thr Asp Ala Ala Thr His Ala His Ile Pro Leu Asn Leu
    130                 135                 140

Pro Val Thr Thr Ala Gln Arg Gln Leu Ser Ser Trp Ala Gln Asn His
145                 150                 155                 160

Trp Gly Thr Phe Trp Gln Leu Ala Asn His Cys Ala Gln Arg Gln Ser
                165                 170                 175

Gln Phe Thr Leu Pro Gln Arg Gly Thr Glu Tyr Thr Ala His Pro His
            180                 185                 190

Leu


<210>  149
<211>  195
<212>  PRT
<213>  Homo sapiens

<400>  149

Ile Leu Asp Ser Phe Arg Asp Phe Leu Glu Gln Gly Gln Glu Ser Phe
1               5                   10                  15

Leu Asp Lys Val Arg Ser Asp Leu Ser Gln Gly Arg Ser Ile Phe Ser
            20                  25                  30

Tyr Thr Arg Arg Asn Phe His His Lys Gln Cys Pro Lys Asp Ala Cys
        35                  40                  45

Tyr His Phe Tyr Ser Met Leu Phe Ser Val Phe Trp Pro Ile Leu Leu
    50                  55                  60

Glu Ile Gln Val Arg Lys Met Thr Lys Gly Ile His Glu Thr Arg Ser
65                  70                  75                  80

Leu Phe Arg Arg Trp Tyr Asp Cys Leu Ser Arg Lys Lys Glu Met Thr
                85                  90                  95

Pro Ser Phe Trp Glu Phe Thr Asn Ser Gly Trp Val Leu Asp Lys His
            100                 105                 110

Leu Lys Asn Gln Ser Phe Pro Cys Val Ala Ala Ile Thr Ile Lys Met
        115                 120                 125

Glu Met Arg Ser Gly Ala Val Asn Ile Gln Gln Glu Leu Leu Ile Cys
    130                 135                 140

Arg Pro Asp Lys Ser Pro Pro Glu Trp Thr Pro Ala Arg Glu Gly Arg
145                 150                 155                 160

Ser Leu Glu Gly Arg Arg Glu Asp Thr Glu Asp Leu Pro Leu Pro Gln
                165                 170                 175

Glu Ala Pro Arg Glu Arg Ala Thr Thr Val Tyr Ser Ser Arg Leu Trp
            180                 185                 190

Gly Asp Ser
        195

<210>  150
<211>  168
<212>  PRT
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<213> Homo sapiens

<400> 150

Leu Lys Ser Ser Gln Gln Pro Ser Asn Arg Tyr Leu Ser Leu Ile Pro
1 5 10 15

Tyr Pro Cys Ser Ala Ser Pro Pro Ile Thr Met Ala Glu Glu Phe Lys
20 25 30

Pro Leu Ser Lys Ala Ser Thr Val Ile Cys Pro Leu Asp Pro Ile Pro
35 40 45

Ser Ile Phe Leu Phe Ile Glu Thr Phe Ser Met Val Phe Lys His Thr
50 55 60

Leu Leu Ser Leu Leu Leu Asn Arg Gln Met Gln Leu Ile Lys Leu Phe
65 70 75 80

Phe Ser Leu Gly Tyr Cys Pro Ile Ser Leu Leu Pro Phe Met Ala Glu
85 90 95

Leu Leu Glu Arg Val Phe His Asn His Phe Ile Ser Thr Pro Leu Thr
100 105 110

Asp Phe Thr Gln Leu Glu Glu Glu Glu Gly Thr Leu Ile Pro Lys Cys
115 120 125

Pro Ile Lys Pro Asn Pro Leu Lys Val Leu Cys Cys His Asp Gly Cys
130 135 140

Glu His Gly Glu Lys Ile Leu Glu Asp Val Gly Asn His Asp Arg Glu
145 150 155 160

Thr Glu Lys Val Val Lys Gly Phe
165

<210> 151
<211> 121
<212> PRT
<213> Homo sapiens

<400> 151

Thr Gly His Pro Arg Leu Pro Pro Thr Leu Lys Gln Pro Ala Arg Gln
1 5 10 15

Cys Val Thr Tyr Gly Phe Asn Ser Asp Glu Glu Asp Ser Ser Trp His
20 25 30

Gly Leu Leu Arg Thr Leu Asn His Lys Val Ser Arg Asp Arg Arg Thr
35 40 45

Val Pro Thr Ala Ala Thr Pro Arg Trp Val Cys Ser Pro Val Ala Thr
50 55 60

Leu Lys Phe Leu Lys Thr Phe Tyr Gly Val Leu Leu Cys His Leu Gly
65 70 75 80

Trp Ser Ala Val Thr Cys Leu Ile Pro His Leu Ala Glu Thr His Arg
85 90 95

Arg Ser Leu Val Arg Thr Arg Glu Gly Ala Gly His Ser Gly Ser Cys
100 105 110

```
Gln His Phe Gly Arg Leu Arg Gln Glu
        115                 120

<210>  152
<211>  211
<212>  PRT
<213>  Homo sapiens

<400>  152

Leu Val Ala Ile Ser Leu Lys Phe Phe Phe Cys Arg Lys Ile Ser His
1               5                   10                  15

Arg Trp Leu Ile Ile Cys His Ile Lys Pro Leu Arg Lys Lys Gly Trp
            20                  25                  30

Gln Met Leu Leu Leu Val Arg Leu Leu Cys Tyr Glu Ile Trp Val Lys
        35                  40                  45

Cys Ala Gly Val Thr Glu Glu Gly Glu Phe Leu Ser Pro Ser Arg Ile
    50                  55                  60

Glu Glu Asn Gly Val Arg Asp Arg Glu Gln Leu Ala Arg Lys Ala Gln
65                  70                  75                  80

Gly Val Asn Leu Thr Arg Lys Phe Lys Gln Trp Leu Leu Leu Tyr Ser
                85                  90                  95

Leu Phe Val Gln Ile Leu Lys Met Lys Leu Phe Ile Lys Phe Ile Val
            100                 105                 110

Val Phe Leu Asn Ser Met Arg Asn Gly Arg Asn Leu Arg Tyr Cys Ser
        115                 120                 125

Lys Gly Ser Ser Ala Pro Asn Leu Phe Leu Thr Lys Phe Ile Leu Leu
    130                 135                 140

Pro Lys Val Ser Pro Asn Val Thr Pro Thr Ser Ile Arg Gln Glu Tyr
145                 150                 155                 160

Cys Asn Glu Ala Met Thr Ile His Asn Leu Leu Ser Ile Lys Gln Val
                165                 170                 175

His Glu Arg Phe Cys Asn Asn Thr Leu Cys Lys Ser Leu Trp Asn Asn
            180                 185                 190

Asn Lys Ile Asp Val His Phe Met Tyr Tyr Cys Ile Leu His Ile Leu
        195                 200                 205

Arg His Glu
    210

<210>  153
<211>  173
<212>  PRT
<213>  Homo sapiens

<400>  153

Val Asp His Trp Ile His Leu Asp Met Phe Lys Met Phe Thr Tyr Gly
1               5                   10                  15

Val Leu Ile Leu Leu Gly Pro Glu Asn Ala Tyr Ser Gly Ile Leu Leu
            20                  25                  30
```

Ser Ser Gly Lys Arg Ala Pro Phe Ser Pro Asn Leu Lys Asp His Glu
35 40 45

Asn His Leu Lys Cys Leu Leu Glu Val Arg Ile Pro Gln Pro Val Trp
50 55 60

Gly Pro Ala Ile Cys Ile Phe Lys Glu Thr Trp Thr Val Thr Cys Glu
65 70 75 80

Lys Pro Tyr Ala Gln Tyr Val Leu Ala Ile Arg Ile Thr Met Val Asn
85 90 95

Ile Asn Tyr Leu Phe Arg Glu His Lys Phe Leu Leu Thr Gln Leu Asn
100 105 110

Ala Lys Cys Phe Lys Ser Lys Thr Pro Cys Leu Lys Asn Ile Gly Phe
115 120 125

Phe Phe Lys Gln Tyr Lys Thr Gly Tyr Leu Ser His Glu Phe Gly Ala
130 135 140

Pro Asn Ser His Cys Phe Gln Thr Ile Ser Gln Glu Arg Ser Leu Gln
145 150 155 160

Ser Pro Pro Val Ala Ser Ile Ala Leu Cys Val Leu Lys
165 170

<210> 154
<211> 172
<212> PRT
<213> Homo sapiens

<400> 154

Gln Ile Leu Gly Ser Lys Arg Arg Lys Met Ser Arg Met Lys Arg Tyr
1 5 10 15

Leu Ile Ile Ser Ser Ala Asp Phe Leu Gly Asn Val Phe Ile Pro Ile
20 25 30

Phe Ile Thr Tyr Val Val Lys Asp Ser Phe Ser Gly Leu Tyr Ile Gln
35 40 45

Leu Phe Glu Tyr Ile Tyr Asn Asn Ile Tyr Ser Cys Leu Ile Gly Asn
50 55 60

Phe Asn Asn Tyr Gln Asn His Lys Glu Ile Phe Phe Ala Cys Phe His
65 70 75 80

Tyr Phe His His Phe Gly Ile Cys Tyr Val Val Lys Lys Tyr Ser Glu
85 90 95

Lys Thr Ile Ile Leu Lys Ser Cys Cys Ile Asn Arg Ile Trp Gly Lys
100 105 110

Glu Gln Thr Thr Lys Arg Gly Arg Leu Met Ser Leu Val Gly Thr Trp
115 120 125

Glu Val Thr Leu Ile Ser His Phe Leu Asn Leu Lys Glu Glu Lys Val
130 135 140

Lys Leu Ile Asn His Ser Thr Gln Lys Asn Thr Phe Trp Thr Ile Lys
145 150 155 160

Asp Ser Ala Ile Tyr Met Asp Tyr Ile Phe Ile Ser

165 170

<210> 155
<211> 231
<212> PRT
<213> Homo sapiens

<400> 155

Arg Cys Glu Pro Leu Pro Gly Leu Glu Leu Leu Leu Asp Cys Ile Pro
1 5 10 15

Arg Gly Asn Phe Met Thr Glu Phe Arg Ser Ala His Ile Leu Ala Ala
20 25 30

Ser Lys Arg Glu Arg Glu Ser Pro Ala Leu Ile Ser Val Ile Phe Leu
35 40 45

Phe Asp Leu Ile Tyr Ser Ile Asn Thr Pro Gln Glu Gly Thr Phe Pro
50 55 60

Ser Pro Ala Pro Lys Gln Asn Arg Ser Ile Leu Asp Gly Leu Pro Asn
65 70 75 80

Trp Cys Leu Gln Thr Ser Ser Leu Ser Pro Ser Pro Thr Leu Lys Ser
85 90 95

Arg Ser Leu Ile Cys Met Gly Cys Ile Ser Thr Leu Met Leu Pro Gly
100 105 110

Phe Trp Leu Gly Leu Pro Asn Gly Arg His His Trp Arg Arg Met Glu
115 120 125

Val Gly Gly Gly Arg Trp Glu Gly Arg Gly Trp Gly Ile Val Pro Leu
130 135 140

Ala Pro Phe Leu Cys Ser Phe Gly Ser Leu Gln His Pro Val Thr Leu
145 150 155 160

Ser Leu Ser His Gln Val Phe Ile Phe Cys Trp Phe Pro Phe Val Leu
165 170 175

Pro Thr Phe Thr Thr Cys Pro Phe Leu Lys Asp Pro Ser Ile Ala Leu
180 185 190

Phe Gly Asn Ile Leu Phe Ser Ala Gly Thr Pro Glu Leu Tyr Arg Arg
195 200 205

Val Gln Glu Ala Thr Lys Leu Gln Met Pro Thr Thr Trp Trp Asn Arg
210 215 220

Cys Pro Leu Glu Ala Ala Ala
225 230

<210> 156
<211> 160
<212> PRT
<213> Homo sapiens

<400> 156

Pro Ile Cys Leu Asn Ala Ser Cys Ser Gly Gly Leu Thr Pro Ile Asn
1 5 10 15

Pro Ser Cys Leu Trp Lys Gly Leu Pro Thr Glu Leu Asp Ser Asn Ile

```
            20                  25                  30

Gln Ser Ser Ser Thr His Pro Phe Ser Trp Thr Leu Trp Gly Pro Arg
        35                  40                  45

Gln Gln Thr Ser Cys Leu Phe Tyr Arg Ala Ala Leu Gln Met Ala Gly
    50                  55                  60

Ala Thr Val Phe Ser Ala Leu Glu Asp Leu Ser Met Val Val Ser Phe
65                  70                  75                  80

His Ile Ser Tyr Asp Phe Tyr Ser Gln Glu Ser Leu Ile Cys Leu Leu
                85                  90                  95

Met His Phe His Leu Ser Val Thr Leu Leu Gln Asn Gln Arg Glu Ile
            100                 105                 110

Thr Leu Ile Phe Leu Arg Ala Ser Lys Leu Pro Gly Leu Gln Arg Pro
        115                 120                 125

Cys Arg Ala His Arg Gln Arg Met Thr Arg Gly His Met Pro Cys Met
    130                 135                 140

His Phe His Leu Ser Val Thr Leu Leu Gln Ala Asn Leu Lys Gly Met
145                 150                 155                 160

<210>  157
<211>  225
<212>  PRT
<213>  Homo sapiens

<400>  157

Val Pro Leu Val Asn Pro Glu Tyr Asn Ile Phe Tyr Lys Thr Cys Phe
1               5                   10                  15

Ile Leu Ser Gly Met Arg Cys Ile Phe Glu Gly Leu Leu Lys Leu Ala
            20                  25                  30

Ile Thr Ile Arg Leu Leu Leu Asn Leu Gly Ile Ser Leu Pro Ser Cys
        35                  40                  45

Gln Gly Leu Tyr Leu Met Phe Val Ser Leu Lys Lys Lys Arg Asn Gln
    50                  55                  60

Thr Asp Tyr Thr Leu Leu Lys Thr Glu Asp Met Tyr Phe Asn Met Ser
65                  70                  75                  80

Leu Leu Pro Val Ile Gln Ser Leu Lys Phe Gln Asn Pro Ser Gly Thr
                85                  90                  95

Leu Cys Gly Pro Trp Ile Lys His Thr Trp Ala Tyr Glu Cys Val Asp
            100                 105                 110

His Trp His Met Arg Gly Asn Cys Leu Leu Gly Tyr Val Ala Leu Pro
        115                 120                 125

Leu Ser Ile Tyr Asn Ser Asn Val Ser Glu Arg Ser Ser Ser Leu Lys
    130                 135                 140

Leu Phe Ser Arg Ile Arg Gln Thr Val Pro Ala Asn Gln Gly Asp Glu
145                 150                 155                 160

Phe Trp Pro Met Phe Gly Arg Ser Leu Leu Gln Trp Gly Val Thr Ser
                165                 170                 175
```

His Glu Arg Ile Ile Arg Asn Leu Ser Thr Thr Leu Gly Asn Leu Ala
180 185 190

Asn Glu Leu Ala Glu Ala Ile Ala Thr Lys Arg Ser Ser Asp Ser Leu
195 200 205

Asp Arg Ile Val Met Asp Asp Gly Ile Thr Leu Gly Tyr Ile Val Val
210 215 220

Lys
225

<210> 158
<211> 215
<212> PRT
<213> Homo sapiens

<400> 158

Leu Pro His Leu Cys Cys Ser Leu Leu Thr Ile Lys Pro Asp Met Cys
1 5 10 15

Leu Ser Pro Cys Leu Pro Thr His Pro Leu Ile Thr Ser Val Pro Cys
20 25 30

Ser Gln Val Ala Ser Arg Glu Asp Cys Gly Leu Met Ser Ser Phe Met
35 40 45

Pro Trp Leu Leu Leu Ile Arg Ala Leu Tyr Thr Phe Ser Lys Ala Leu
50 55 60

Glu Ser Lys Lys Val Leu Leu Gly Ser Ser Pro Gln Met Gln Phe Met
65 70 75 80

Lys Ser Val Ser Phe Ser Phe Pro Ser Glu Phe Leu Ser Val Ser Ile
85 90 95

Lys Ala Leu Asp Thr Pro Trp Phe Thr Arg Gln Lys Leu Ile His Pro
100 105 110

Thr Gln Pro His Gly Tyr Ser Phe Val Leu Leu Asp Asn Asn His Leu
115 120 125

Arg Lys Pro Asp Leu Phe Pro His Ser Ser Phe Ser Phe Cys Pro Ala
130 135 140

Glu Asn Lys Arg Thr Ser Cys His Ile Val Ile Cys Ser Ala Leu Leu
145 150 155 160

Leu Arg Ser Leu Val Gly Lys Thr Gly Pro Ile Lys Arg Asp Thr Ala
165 170 175

Met Pro Trp Gly Glu Asp Asn Lys Ser Asp Gly Ser Arg Ala Leu Glu
180 185 190

Ser Arg Gly Gly Val Thr Asn Cys Pro Asn Gly Thr Val Pro Ser Glu
195 200 205

Leu Leu His Leu Leu Leu Thr
210 215

<210> 159
<211> 202
<212> PRT

<213> Homo sapiens

<400> 159

Leu Lys Val Lys Lys Glu Tyr Pro Phe Ile Leu Asp Asn Cys Cys Gln
1 5 10 15

Arg His Tyr Asn Ile Ser Val Val Ile Pro Tyr Phe Ser Lys Ala Lys
20 25 30

Ile Glu Ile Trp Pro Leu Leu Leu Cys Asn Phe Leu Lys Phe Lys Val
35 40 45

Ser Val Phe Ser Ile Ile Lys Tyr Ser Ser Leu Lys Leu Met Ala Ile
50 55 60

Arg Tyr Ser Ile Val Trp Ile Ile Tyr Leu Arg Phe Cys Gly Leu Phe
65 70 75 80

Cys Phe Gln Asn Asn Thr Lys Ile Asn Ile Phe Val Cys Lys Tyr Phe
85 90 95

Thr Lys Ile Tyr Ser Glu Lys Phe Leu Lys Val Glu Phe Leu Gly Glu
100 105 110

Val Thr Phe Lys Cys Leu Ile His Leu Leu Ser Gly Lys Thr Val Arg
115 120 125

Phe Leu His Ser His His Ser Val Tyr Gly His Gln Leu Thr Val Phe
130 135 140

Phe Pro Thr Leu Leu Ile Phe Ser Leu Ser Met Trp Ile Lys Phe Gly
145 150 155 160

Phe Tyr Tyr Phe Asn Leu Tyr Ser Ile Thr Leu Leu Ala Ile Ser Leu
165 170 175

Gly Val Val Asn Ile Cys Pro Cys Pro Phe Leu Phe Gly Met Leu Ser
180 185 190

Leu Met Thr Asn Cys His Asn Val Ile Asn
195 200

<210> 160
<211> 215
<212> PRT
<213> Homo sapiens

<400> 160

Asn Ile Ser Phe Leu Ser Leu Lys Met Ala Val Ser Cys Val Leu Ile
1 5 10 15

Asn Leu Lys Ile Asn Leu Ser Ile Gly Glu Ala Gly Lys Leu Ala Trp
20 25 30

Lys Val Asn Leu Leu Ser Arg Gly Lys Ile Ser Trp Ala Leu Ile Lys
35 40 45

Val Asp Ile Phe Arg Gly Gly Lys Ser Lys Phe Tyr His Thr Leu Ala
50 55 60

Phe Val Gln Phe Ser Pro Leu Phe Ser Leu Tyr Tyr Leu Phe Phe Cys
65 70 75 80

Phe Thr Leu Gly Lys Ala Asn Tyr Leu Phe Ser His Ile Phe Trp Gly
85 90 95

Pro Ile Leu Met Ile Leu Ile Phe Phe Ser Cys Leu Thr Cys Arg Pro
100 105 110

Ser Thr Glu His Cys Arg Ala Ser Ser Gln Arg Ser Ser Gly Asp Glu
115 120 125

Leu Ser Phe Leu Gly Trp Asp Cys Cys Ala Gly Leu Asp Arg Thr Glu
130 135 140

Asn Cys Arg Asp Lys Tyr Thr Tyr Glu Gln Thr Ser His Leu Phe Ile
145 150 155 160

Lys Ala Leu His Trp Leu Trp Lys Thr Ala Val Gly Leu Arg Lys Leu
165 170 175

Asn Phe Leu Gly Ile Phe Val Leu Asn Ile Glu Arg Glu Arg Arg Arg
180 185 190

Phe Leu Phe Lys Arg Val Tyr Glu Thr Leu Ser Leu Lys Ser Asn Leu
195 200 205

Met Thr Gly Cys Met Cys Ser
210 215

<210> 161
<211> 199
<212> PRT
<213> Homo sapiens

<400> 161

Lys Ile Gln Ile Leu Cys His Ser Pro Ala Tyr Leu Leu Thr Leu Pro
1 5 10 15

Leu Leu Ser Lys Phe Ile Ile Leu Thr Val Val Val Asn Ala Leu Leu
20 25 30

Ser Val Pro Cys Pro Phe Val Tyr Thr His Leu Val Leu Leu Ser Phe
35 40 45

Phe Ile Asn Met Leu His His Thr Val Ile Phe Leu Leu Ile Phe Phe
50 55 60

Lys Lys Val Trp Asn Ile Ser Phe Pro Leu Cys Val Leu Cys Asn Leu
65 70 75 80

Ser Asp Lys Thr Thr Cys Tyr Ile Phe Ser Thr His Asn Phe Ile Ser
85 90 95

Gly Leu Cys Ala Leu Tyr Lys Ser Thr Asn Leu Ser Val Trp Ser Val
100 105 110

Leu Ser Ser Pro Gly Gln Ile Leu Ile Ile Cys Gln Glu Cys Asn Ser
115 120 125

Ile Ile Ser Ser Val Thr Gln Phe Ser Lys His Arg Ile Leu Cys Val
130 135 140

Pro Ile Ala Leu His Trp Ile Gly Pro Gln Phe Cys Gln Cys Ile Ile
145 150 155 160

Arg Thr Tyr Leu Gln Val Leu Ser Leu Leu Leu Trp Arg Glu Pro Phe

165 170 175

Ser His Met Asn Cys Asp Phe Val Tyr Leu Ala Pro Thr Met Val Leu
180 185 190

Asn Ser Trp Val Leu Gly Lys
195

<210> 162
<211> 213
<212> PRT
<213> Homo sapiens

<400> 162

Tyr Trp Phe Asn Lys Leu Trp Tyr Asn Gln Ile Met Lys Leu Tyr Ala
1 5 10 15

Phe Val Lys Val Thr Phe Gln Lys Asn Ile Leu His Arg Ile Thr Asp
20 25 30

Pro Ser Ala Leu Pro Thr Leu Trp Ala Leu Ser Leu Phe His His His
35 40 45

Tyr Leu His His Cys Leu Gln Val Phe Tyr Thr Ala Arg Val Gly Leu
50 55 60

Cys Leu Leu Asn Ser Gln Val Lys Arg Gly Arg Lys Leu Thr Pro Ser
65 70 75 80

Gly Gly Ser Leu Gly Met Ile His Gly Arg Trp Ser Ile Asn Thr Ser
85 90 95

Ala Leu Phe Pro Leu Glu Ile Leu Arg Asn Gly Phe Tyr Ile Val Ser
100 105 110

Gln Ser Phe Leu Lys Val Leu Asn Phe Asn His Pro Gln Gly Trp Ala
115 120 125

Leu Ser Tyr Thr Ser Phe Val Ala Ser Leu Pro Ser Cys Leu Thr Ser
130 135 140

Pro Phe Gln Thr Arg Ile Tyr Phe Phe Ser Leu Lys Gln Asn Lys Met
145 150 155 160

Phe Asn Leu Lys Pro Leu Gln Asn Thr Asn Leu Tyr Leu Lys Asn Leu
165 170 175

Asn Ile Gly Glu Asn Glu Thr Val Tyr Ala Gln Val His Asp Trp Trp
180 185 190

Arg Leu Lys Ser Ser Lys Ile Phe Leu Lys Gly Tyr Pro Ser Arg Arg
195 200 205

Leu Asn Cys Leu Ile
210

<210> 163
<211> 236
<212> PRT
<213> Homo sapiens

<400> 163

Leu Ala Ser Glu Ser Leu Leu Val Arg Lys Glu Val Val Leu Phe Pro

1 5 10 15

Leu Gln Ala Lys Ala Phe Gln Val Leu Ser Phe Cys Ser Ile Lys Arg
20 25 30

Gln Leu Arg Gly Arg Tyr Pro Gln Glu Phe Pro Asp Ser Cys Thr Asp
35 40 45

Leu Ser Ala Glu Ile Ala Glu Val Ser Trp His Leu His Glu His Leu
50 55 60

Ser Val Ala Gly Arg Ile Asn Gly Lys Arg Ala Thr Glu Ile Pro Gly
65 70 75 80

Ala Lys Ser Ser Ser Glu Ser Pro Ile Phe Asp Gln Glu Leu Val Gly
85 90 95

Ser Leu Arg Ile Cys Ile Ser Ser Asp Ser Arg Leu Ser Gly Leu Ser
100 105 110

Asn Trp Asp Gln Ser Asn Ser Tyr His Ala Tyr Leu Val Pro Gly Ser
115 120 125

Leu Leu Arg Ala Ser Trp Thr Pro Ala Arg Val Ser Pro His Ser Asn
130 135 140

His Met Arg Tyr Val Leu Leu Leu Ser Pro Cys Ala Asp Glu Asp Thr
145 150 155 160

Arg His Arg Glu Asn Trp Pro Gln Val Tyr Ser Trp Gly Gly Gln Ser
165 170 175

Gln Asn Ser Asp Leu Gly Cys Leu Gly Cys Glu Leu Val Trp Ala Ser
180 185 190

Met Gly His Arg Gly Arg Ile Ser Trp Arg Ser Arg Thr Glu Gly Lys
195 200 205

Arg Asp Glu Ile Ser Asp Ser Ala Gly Ser Glu Thr Leu Ser Ala Met
210 215 220

Ile Lys Pro Asp Tyr Gly Thr Cys Phe Ser Leu Ser
225 230 235

<210> 164
<211> 193
<212> PRT
<213> *Homo sapiens*

<400> 164

Phe Gln Asp Ile His His Arg Cys Gly Arg Gly Lys Lys Thr Met Gly
1 5 10 15

Met Gly Ile Leu Pro Phe Ile Asn Thr Gly His Phe Asn Leu Leu Asn
20 25 30

Leu Ser Thr Phe Cys Asn Leu Arg Ile Phe Ile Leu Asp Ser Trp Thr
35 40 45

Lys Ala Leu Glu Met Ala Ser Phe Ala Arg Phe Leu Cys Ala Leu Glu
50 55 60

Lys Ile Pro Gly Phe Asn Ala Lys Asn Arg Gln Gln Arg Ala Gln Glu
65 70 75 80

Met Glu Leu Ser Gly Val Leu Leu Gln Leu Arg Thr Val Cys Tyr Ser
85 90 95

Pro Phe Lys Ile Ser Pro Asn Leu Tyr Leu Met Val Lys Asp Val Phe
100 105 110

Phe Phe Leu Leu Glu Glu Lys Val Thr Arg Ile His Gly Ser Gly Leu
115 120 125

Ile Val Leu Leu Leu Met Glu Ile His Lys Gln Phe Leu Lys Tyr Ser
130 135 140

Leu Ala Ser Glu Leu Val Trp Asn Leu Ala Val Tyr Leu Leu Asp Trp
145 150 155 160

Val Thr Thr Ala Val Ala Gly Ser Ile His Tyr Thr Arg Leu Cys Ile
165 170 175

Ser Met Met Ile Val Lys Phe Cys Glu Lys Val Leu His Leu Cys Ser
180 185 190

Leu

<210> 165
<211> 199
<212> PRT
<213> Homo sapiens

<400> 165

Leu Phe Ser Ala Phe Ser Leu Ile Leu His Leu Thr Gly Leu Val Val
1 5 10 15

Asn Ile Leu Lys Val Tyr Val Leu Ile Lys Thr Ser Ser Phe Pro Lys
20 25 30

Glu Lys Lys Ser Gln Phe Gly Leu Val Ser Leu Ser Cys Phe Leu His
35 40 45

Leu Thr Asn Val Ser Phe Ile Tyr Ser Phe Cys Ser Val Thr Phe Arg
50 55 60

Met Ile Leu Met Gly Lys Asn His Gly Ser Tyr Lys Gln Pro Phe Lys
65 70 75 80

Thr Ile Val Ile Leu Cys Ser Val Asp Ser Gly Arg Gly Phe Lys Val
85 90 95

Ile Ile Ser Leu Lys His Cys Val Asn Ile Pro Pro Thr Val Val Pro
100 105 110

Leu Gly Thr Gly Lys Ile Gln Asn Trp Pro Ala Ser Ser Leu Thr Arg
115 120 125

Val Ile Lys Val Arg Leu Leu Tyr Ile Lys Gln His Leu Asn Ala Trp
130 135 140

Cys Val Ala Ala Gly Lys Gln Pro Arg Ser Pro Ser Cys Ile Arg Gly
145 150 155 160

Leu Met Asn Val Ser Ile Ala Val Phe Ala Val Thr Arg Ser Gly Arg
165 170 175

Val Phe Pro Ser Ser Leu Asp Cys Leu Pro Met His Thr Gly Val Cys
180 185 190

Ile Gly Lys Gln Ser Arg Leu
195

<210> 166
<211> 150
<212> PRT
<213> Homo sapiens

<400> 166

Ile Trp Cys Phe His Arg Leu Lys Gly Leu Arg Cys Pro Pro Val Ala
1 5 10 15

Val Ala Cys Gly Ser Leu Cys Ser Cys Leu Pro Ser Trp Ala Gln Tyr
20 25 30

Leu Val Leu Cys Leu Gly Phe Thr Asn Ala Thr Asn Thr Tyr Ala Pro
35 40 45

Thr Leu Cys Gln Val Leu Cys Tyr Met Leu Arg Lys Gln Cys Thr Arg
50 55 60

Trp Ile Arg Phe Ser Ser Leu Trp Cys Pro Ser Ser Gly Lys Asp Arg
65 70 75 80

Leu Ser Val Phe Tyr Gly Gln Ala Tyr Arg Ala Lys Lys Thr Cys Val
85 90 95

Gly Met Gly Gln Gly Arg Tyr Pro Trp Ser Ser Pro Val Thr Gly Ile
100 105 110

Arg Leu Arg Val Ile Val Gly Arg Ala Leu Gln Ala Gly Gly Ser Ala
115 120 125

Cys Ala Arg Val Leu Arg Lys Glu Gly Glu Gln Cys Val Arg Asn Ile
130 135 140

Thr Val Val Ala Thr Gln
145 150

<210> 167
<211> 218
<212> PRT
<213> Homo sapiens

<400> 167

Ile Ile Ile Arg Ile Ile Arg Ile Leu Lys Tyr Pro Asn Asn Gln Val
1 5 10 15

Asn Lys Ala Thr Phe Tyr Gly Ile Ile His Phe Cys Phe Glu Lys Tyr
20 25 30

Thr Leu Phe Lys Tyr Tyr Cys Leu Phe Thr Gln Leu Leu Glu His Ser
35 40 45

Ser Ala Lys Ala Phe Met Ile Phe Thr Asn Leu Ala Phe Ile Phe Ala
50 55 60

Leu Leu Ser Thr Ile Thr Lys Val Ile Thr Thr Cys Ser Pro Thr Asn
65 70 75 80

Tyr Ser Asp Gly Ala Leu Arg Ile Asp Leu Tyr Leu Asn Ile Leu Trp
85 90 95

Tyr Gln Val Phe Leu His Ser Ser Arg Ile Phe His Phe Ala Tyr Ile
100 105 110

Leu Met Met Ser Ser Arg Ile Ser Ser Leu Thr Tyr Leu Ala Asn Tyr
115 120 125

Lys Tyr Val Ile Phe Val Lys Tyr Leu Arg Val Cys Ser Ala Ile Tyr
130 135 140

Leu Val Ile Leu Asn Gln Ile Leu Asn Val Tyr Thr Phe Leu Met Tyr
145 150 155 160

Asn Phe Gln Phe Phe Arg Met Arg Leu Asn Asn Cys Pro Tyr Tyr Ser
165 170 175

Phe Ile Thr Thr Leu Ile Tyr Leu Leu Tyr Leu Gln Met Ile Tyr Lys
180 185 190

Asn Ala Phe Leu Tyr Leu Ser Leu Ser Gln Val Leu His Ser Glu Leu
195 200 205

Phe Phe Leu Phe Val Phe Leu Arg Tyr Ile
210 215

<210> 168
<211> 204
<212> PRT
<213> Homo sapiens

<400> 168

Tyr Cys Glu Leu Arg Cys Tyr Ile Ser Glu Cys Asn Glu Trp Asp Ile
1 5 10 15

Ala His Trp Leu Glu Lys Pro Pro Lys Gln Ala Ala Ser Ala Ile Glu
20 25 30

Leu Leu Ala Trp Ser Arg His Ser Ala Ser Gly His Gly Asp Asn Ser
35 40 45

Ser Glu Ile Asn Ser Ser Thr Lys Val Ser Asn Asp Val Ile Ser Ser
50 55 60

Gln Arg Gln Gly Cys Pro Val Lys Gln Thr Asp Gly Gln Ser Pro Pro
65 70 75 80

Arg Leu Lys Gly Gly Gly Glu Thr Gly Arg Lys Arg Met Arg Trp Val
85 90 95

Arg Lys Arg Tyr Asn Leu Arg Val Thr Met Ser Ser Cys Ser Pro Arg
100 105 110

Trp Gln Trp Val Gly Gly Pro Gly Lys Asp Cys Phe Arg Gln Met Glu
115 120 125

Gln Cys Met Arg Arg Ser Arg Glu Lys Ser Gln Ile Val Cys Ile His
130 135 140

Val Leu Gln Asn Arg Glu Ser Asn Arg Tyr Leu Gly Lys Lys Lys Glu
145 150 155 160

Val Ser Leu Phe Leu Ser Leu Lys Val Gln Lys Trp Ala Phe Pro Gln

165 170 175

Phe Ile Cys Gln Pro His Glu Val Phe Thr Asp Leu Asp Leu Leu Ile
180 185 190

Ser Cys Tyr Phe Ile Thr Leu Leu Glu Leu Leu Pro
195 200

<210> 169
<211> 158
<212> PRT
<213> Homo sapiens

<400> 169

Lys Val Leu Ile Phe Val Leu Arg Pro Ile Tyr Thr Tyr Lys Cys His
1 5 10 15

Pro Ser Ile Phe Leu Cys Asn Phe Leu Ser Ala Gly Leu Pro Ser Leu
20 25 30

Met Cys Val Leu Tyr Phe Pro Tyr Ile Cys Tyr Pro Ile Thr Cys Phe
35 40 45

Tyr Asn Cys Leu Phe Tyr Phe Pro Phe Phe Ser His Cys Leu His Ala
50 55 60

Leu Phe Leu Val Leu Asn Ser Ile Thr Leu Ile His Cys Ser Ser Asn
65 70 75 80

Phe Ile Leu Asn Asn Phe Pro Ile Tyr Leu Asp Ile Tyr Leu Asn Val
85 90 95

His Ile Ser Pro Leu Ile Glu Val Cys Leu Val Ile Phe Gly Met Met
100 105 110

Leu Asn Leu Phe Leu Trp Lys Gly Thr Asn Thr Cys Met Phe Met His
115 120 125

Val Gln Lys Cys Ser His Arg Met Ile Ile Lys Ala Asp Leu Gly Lys
130 135 140

Lys Thr Ser Leu Ile Phe Ile Phe His Ile Arg Phe Phe Glu
145 150 155

<210> 170
<211> 198
<212> PRT
<213> Homo sapiens

<400> 170

His Gln Asn Ser Pro Ile Tyr Leu Arg Ile Asn Val Asn Phe Glu Phe
1 5 10 15

Asp Ile Thr Met Ile Lys Gly Ala Leu Ile Phe Ser Arg Ser Tyr Lys
20 25 30

Ile Phe Val Asn Glu Leu Ile Gly Arg Ile Cys Leu Leu Lys Ser Glu
35 40 45

Val Gly Gly Glu Leu Lys Leu Gly Leu Ile Gly Asn Tyr Ile Trp Val
50 55 60

Met Asn Ala Trp Gly Phe Ile Ile Pro Leu Pro Leu Pro Leu Ser Val

65 70 75 80

Phe Glu Leu Cys His Cys Glu Asn Ile Val Leu Lys Ala Val Leu Phe
85 90 95

Phe Leu Leu Arg Gly Ser Lys Lys Ser Lys Lys Tyr Thr Gly Leu Ile
100 105 110

Glu Tyr Val Cys Ser Asn Lys Ile Pro Gly Phe Ser Phe Val Leu Ala
115 120 125

Ser Arg Asn Gln Val Gln Phe Val Ser Lys Asp Phe Ala Thr Cys Gly
130 135 140

Gly Lys Leu Leu Gln Asp Leu Ile Val His Ser Gln Arg Leu Ser Ala
145 150 155 160

Ala Arg Gln Ala Ala Phe Tyr Glu Asn Asp Asn Gln Lys Ala Gly Ala
165 170 175

Leu His Thr Gly His Ser Ser Asn Glu Ser Trp Asp Leu Asp His Gly
180 185 190

Ser Leu Thr Trp Ala Ala
195

<210> 171
<211> 176
<212> PRT
<213> Homo sapiens

<400> 171

Leu Lys Val His Val Leu Ile Tyr Ile His Gln Ile Thr Thr Thr Ser
1 5 10 15

Ser Phe Leu Phe Ile Ser Leu Leu Pro Phe Ile Ser Phe Ile His Met
20 25 30

Leu Ser Leu Asn Thr Leu Leu Leu Leu Leu Thr Val Ile Phe Gln Ile
35 40 45

Ser Glu Lys Asn Leu Ile Leu Pro Tyr Ser Thr Phe Leu Met Leu Phe
50 55 60

Leu Phe Tyr Ala Val Leu Phe Asp Ile Ser His Arg Ala Gly Gln Leu
65 70 75 80

Ala Met Asn Tyr Ser Ser Phe Val Cys Gln Lys Ile Ser Leu Phe Leu
85 90 95

Ile Arg Ile Ile Leu Leu Asn Ala Glu Phe Gly Ser Phe Phe Val Ala
100 105 110

Thr Leu His Val Phe Ser Phe Leu Cys Val Cys Met Val Ser Glu Glu
115 120 125

Lys Asp Asn Val Ile Leu Ile Leu Phe Pro Leu Trp Ile Arg Cys Trp
130 135 140

Leu Phe Pro Leu Ser Ser Phe Phe Gln Asp Phe Leu Phe Ser Leu Val
145 150 155 160

Phe Cys Ser Leu Asn Met Ile Cys Leu Gly Gly Asp Leu Asp Leu Leu
165 170 175

<210> 172
<211> 195
<212> PRT
<213> Homo sapiens

<400> 172

Ala Tyr Arg Ile Ser Thr Thr Val Phe Ala Lys Glu Lys Ser Val Val
1 5 10 15

Ile Lys Phe Ile Leu Trp Leu Asn Tyr Val Leu Gln Phe Val Gly Pro
20 25 30

Val Thr Cys Gly Arg Gln Arg Ala Val Gly His Ser Val Lys Ala Thr
35 40 45

Thr Arg Val Leu Ser Ile Glu Ser Leu Cys Ile Met Val Leu Ala Arg
50 55 60

His Cys Ser Leu Thr Ser Ile Phe Leu Ser Gln Ser Ser Leu Arg Asn
65 70 75 80

Ala Cys Ser Thr Gly Leu Ile Ile Leu Thr Glu Thr Ser Gly His Phe
85 90 95

Met Ser Tyr Gly Met Leu Ala Glu Asp Ile Lys His Arg Cys Val Gly
100 105 110

Ile Gly Gly Glu Ser Thr Ala Ile Phe Gln Leu Gly Ala Pro Trp Phe
115 120 125

Pro Glu Ile Gln Ser His Gly Val Asn Gln Thr Pro Leu Ser Gly Ala
130 135 140

Leu Cys Ser Thr Gln Asp Pro Thr Leu Ser Gly Lys Leu Lys Thr Lys
145 150 155 160

Ser Leu Leu Tyr Ile Arg Phe Ile Lys Asn Ala Thr Ile Thr Lys Ser
165 170 175

Leu Trp Ala Cys Val Glu Asn Ala Val Ile Lys Leu Asn Ile Lys Ala
180 185 190

Ser Ser Lys
195

<210> 173
<211> 225
<212> PRT
<213> Homo sapiens

<400> 173

Gln Arg Leu Thr Tyr Ser Asn Cys Ile Val Asp Trp Ala His Thr Leu
1 5 10 15

His Val Thr Asn Val Ser Asn Tyr Trp Ile Cys Thr Ala Leu Pro Ala
20 25 30

Gly Leu Arg Met Ala Cys Leu Gly Thr Tyr Ile Leu Cys Leu Gln Arg
35 40 45

Thr Gly His Gly Trp Arg Leu Gly Gly Pro Met Ala Asp Ala Trp Asn
50 55 60

```
Ala Thr Trp Gln Leu Trp Thr Lys Asp Ala Ala Arg His Met Val Cys
65                  70                  75                  80

Pro Thr Pro Gly Trp Pro Ile Ala Phe Met Met Gly Leu Ala Ser Gly
                85                  90                  95

Glu His Val Val Leu Pro Ala Gln Val Pro Gln Cys Ile Glu Gln His
            100                 105                 110

Trp Gly Asn Thr Thr Val Gly Trp Val Pro Val Thr Ala Phe Ala Asn
        115                 120                 125

Ile Thr His Val Thr Thr Lys Val Arg Pro Leu Thr Leu Cys Pro Leu
    130                 135                 140

Gly Val Tyr Gly Ser Val Gly Thr Gln Ser Arg Phe Thr Tyr Pro Thr
145                 150                 155                 160

Ala Leu Asp Ile Val Pro Gly Gly Gly Leu Met Cys Leu Pro Leu Phe
                165                 170                 175

Ser Pro Cys Cys Pro Asp Ala Arg Ile Thr Gly Arg Cys Tyr Thr Leu
            180                 185                 190

Ser Leu Cys Glu Cys Asn Glu Pro Pro Ala Val Leu Pro Phe Gly Ser
        195                 200                 205

Asp Tyr Pro Trp Ser Gly Cys His Asn Cys Arg Ser Thr Gly Tyr Cys
    210                 215                 220

Ser
225

<210>  174
<211>  169
<212>  PRT
<213>  Homo sapiens

<400>  174

Phe Met Ile Gln Gln Ile Lys Cys Gly Asn Tyr Leu Lys Arg Lys Lys
1               5                   10                  15

Lys Asn Ile Trp Glu Ala Ala Glu Met Arg Thr Ile Arg Asn Glu His
            20                  25                  30

Phe Tyr Phe Leu Ser Phe Leu Asn Gly Ala Ser Asp Ala Val Phe Ile
        35                  40                  45

Ala Leu Phe Phe Pro Asn Trp Asn Ile Phe Phe Leu Ile Leu Leu Val
    50                  55                  60

Tyr Ser Leu Val Thr Lys Lys Val Phe Arg Lys Tyr His Asn Phe Pro
65                  70                  75                  80

Asn Ser Leu Leu Ser Ala Gly Asp Tyr Glu Tyr Ile Leu Gln Asn Gly
                85                  90                  95

Lys Gly Gly Ser Ser Gly Pro Ala Thr Ile Cys Ile Leu Lys Asp Leu
            100                 105                 110

Val Glu Leu Lys Ser Gln Arg Lys Trp Glu Glu Leu Ser Lys Tyr Phe
        115                 120                 125
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Ile Ile Phe Phe Leu Glu Tyr Gln Val Leu Ile His His Ile Phe His
130 135 140

His Val Ser Lys Ser Phe Phe Leu Lys Lys Val Cys Ile Tyr Ile Ser
145 150 155 160

Lys Arg Val Ser Val Val Lys Lys Asn
165

<210> 175
<211> 199
<212> PRT
<213> Homo sapiens

<400> 175

Glu Asn Thr Tyr Gly Lys Glu Leu Ser Val Arg Phe Gly Ser Gln Ile
1 5 10 15

Leu Ile Phe Asn Lys Ile Tyr Ile Cys Ser Pro Cys Thr Lys Gly Asn
20 25 30

Ser Thr Glu Ser Met Pro Asn Ser Lys Gly Met Thr Leu Asn Leu Tyr
35 40 45

Ser Lys Tyr Ile Gly Pro Ala Ile Leu Cys Gln Met Leu Tyr Leu Tyr
50 55 60

Leu Ile Ala Thr Arg Thr Gly Asn Cys Ala Gln Leu His Leu Arg Thr
65 70 75 80

Val Ser Ile Leu Lys His Thr Ser Tyr Ser Ser Ser Asp Pro His Trp
85 90 95

Met Lys Leu Asn Gln Thr Lys Gln Lys Ser Tyr Leu Ser Pro Asn Asn
100 105 110

Glu Arg Val Cys Arg Met His Ile Val Arg Leu Thr Asp Pro Phe Arg
115 120 125

Gln Tyr Val Gly Phe Pro Arg Ile Leu Ser Ala Ser Lys Gln Phe Glu
130 135 140

Phe Ser Ser Ala Leu Met Ile Trp Phe Pro His Leu Asp Gly Pro Gly
145 150 155 160

Ser Asp Ala Arg Gly Pro His Glu Met Ser Trp Ala Phe Ile Gln Asp
165 170 175

Pro Val Ala Pro Ala Gln Glu Asn Arg Pro Leu Arg Val Ser Gly Ser
180 185 190

Glu Met Ala Ser Val Thr Arg
195

<210> 176
<211> 204
<212> PRT
<213> Homo sapiens

<400> 176

Leu Phe Asn Phe Val Phe Val Ala Val Val Cys Ile His Val Cys Trp
1 5 10 15

Cys Pro Tyr Val Leu Phe Gly Val Trp Leu Phe Ser Gln Asn Gln Val
20 25 30

Thr Val Lys Ser Leu Asn Phe Ser Ile Ser Leu Leu Ser Ser Gly Thr
35 40 45

Val Thr Val Cys Leu Leu Leu Lys Ser Phe Val Phe Leu Thr Arg Gly
50 55 60

Glu Val Tyr Ser Thr Leu Thr Gly Leu Tyr Phe Gly Leu Arg Pro Tyr
65 70 75 80

Lys Thr Phe Leu Lys Ser Leu Ile Ile Cys His Ile Ile Lys Lys Leu
85 90 95

Tyr Gly Ile Phe Ser His Tyr Ile Leu Ala Thr Met Pro Val Tyr Ile
100 105 110

Ser Lys Gln Thr Ile Cys Gly Asn Asn Leu Lys Lys Lys Ala Ile Gly
115 120 125

Ser Lys Tyr Leu Ile Lys Tyr Pro Leu Glu Leu Asn Ile Ser Ser Cys
130 135 140

Gly Ser Ser His Thr Lys Tyr Pro Thr Leu Leu Ser Phe Arg Val Leu
145 150 155 160

Ala Gly Thr Gly Ser Ile Lys Asp Asn Glu Leu Lys Lys Gly Thr Ile
165 170 175

Tyr Lys Tyr Val Ala Arg Leu Gly Glu Thr Ser Lys Val Gly Asn Ala
180 185 190

Ala Gln Asp Ser Asn Lys Ser Glu Asn Leu Phe Leu
195 200

<210> 177
<211> 201
<212> PRT
<213> Homo sapiens

<400> 177

His Val Thr Leu Met Ser Thr Val Phe Ser Ser Val Ala Ser Thr Pro
1 5 10 15

Leu Pro Asn Ser Tyr Asp Asn Ser Ala Ser Gln Thr Tyr Gly Leu Arg
20 25 30

Asn Pro Leu Lys Ser Gln Leu Val Met Thr Pro Lys Arg Phe Phe Ile
35 40 45

Ile Ile Leu Tyr Ile Asn Ile Leu Leu Glu Val His Phe Tyr Glu Asn
50 55 60

Asn Leu Phe Ser Lys Ile Ser Glu Lys Asn Ser Ile Ile Leu His Ile
65 70 75 80

Gly Ile Phe Leu Met Pro Gly Leu Ile Glu Asp Asn Ile Phe Met Ser
85 90 95

Thr Ser Gly Phe Asp Leu Phe Gln Tyr Val Ser Leu Val Glu Ile His
100 105 110

Glu Gly Asn Leu Gly Ser Ser Asp Ile Leu Glu Lys Gly Gly Val Phe

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        115                 120                 125

Gln Pro Phe Trp Thr Thr Val Asp Ile Val Leu Tyr Tyr Asn Lys Thr
    130                 135                 140

Gly Glu Val Val Gly Ser Lys Leu Val Ala Thr Trp Asn Leu Lys Pro
145                 150                 155                 160

His His Glu Leu Phe Val Ile Trp His Ile Lys Ile Tyr Leu Ser Ile
                165                 170                 175

Leu His Phe Glu Trp Asp Pro Leu Leu Met His Leu Phe Val Thr Ile
            180                 185                 190

Ile Ser Asn Thr Leu Val His Val Met
        195                 200

<210>  178
<211>  216
<212>  PRT
<213>  Homo sapiens

<400>  178

Ile Lys Ile Pro Ala Val Lys Leu Asp Ser Ala Cys Leu Gly Ile Phe
1               5                   10                  15

Lys Arg Ile Met Tyr Arg Gly Cys His Gly Asn Ser Ser Ser Gly Asn
            20                  25                  30

Ser Val Pro Phe Val Lys Thr Leu Lys Gly Glu Asp Lys Gln Phe Gly
        35                  40                  45

Glu Ile Thr Ala Pro Glu Ile Glu Phe Ile Cys Asn Leu Gly Ser Leu
    50                  55                  60

Val Cys Leu Pro Ala Ile His His Val Asp Glu Lys Gln Lys Asp Lys
65                  70                  75                  80

Lys Asp Ser His Phe Lys Ala Pro Asn Cys Gln Phe His Ser Ile Ala
                85                  90                  95

Asp Ser Gln His Arg Arg Lys Trp Asp Asn Ala Gly Arg His Tyr His
            100                 105                 110

Arg Thr Val Ser Ser Lys Glu Lys Pro Asn Cys Tyr Phe Ser Met Ala
        115                 120                 125

Glu Gly Gly Cys Phe Pro Arg Gly Arg Ile Leu Phe Asn Pro Val Arg
    130                 135                 140

Ala Gln Leu Gln Pro Ser Val Thr Gly Gln Leu Pro Pro Ser Asn Pro
145                 150                 155                 160

Glu Gly Arg His Glu Pro Tyr Ser Arg Thr Gly Ala Cys Ser Leu Leu
                165                 170                 175

Ser Thr Ser Cys Thr Phe Arg Ala Pro Ala Trp Asp Ala Glu Asn Ser
            180                 185                 190

His Pro Ser Arg Ala Ala Glu Asp His Met Thr Asp His Gln Leu Phe
        195                 200                 205

Leu Thr His Leu Ser Thr Thr Thr
    210                 215
```

<210> 179
<211> 189
<212> PRT
<213> Homo sapiens

<400> 179

```
Ser Gln Asn Phe Asp Leu Thr Asn Gln Arg Gly Gly Leu Val Phe Phe
1               5                   10                  15

Tyr Leu Leu Ser Ala Phe Cys Phe Arg Leu Leu Asn Leu Tyr Ile Lys
            20                  25                  30

Thr Cys Tyr Thr His Leu Ala Val Phe Phe Phe Ala Ala Val Thr Ser
        35                  40                  45

Phe Trp Leu Arg Phe Phe Phe Lys Lys Met Tyr Lys Thr Leu Gly Leu
    50                  55                  60

Ile His Cys Ser Phe Phe Val Leu Ile His Pro Gln Glu Arg Lys Trp
65                  70                  75                  80

Leu Ser Leu Tyr Val Phe Lys Gly Leu Cys Glu Leu Leu Lys Ala Ser
                85                  90                  95

Val Thr Ala Arg Thr Ser Val His Lys Gln Val Gln Asp Ala Ala Glu
            100                 105                 110

Gly Val Ser Ser Leu Thr Glu Arg Gly Ile Glu Leu Phe Arg Met Phe
        115                 120                 125

Cys Val Gly Thr Asp Arg Leu Lys Ala Thr Asp Leu Met Glu Val Trp
    130                 135                 140

Ser Phe Gln Gln Met Ser Ser Asn Leu Thr Asn Leu Asp Leu Val Phe
145                 150                 155                 160

Pro His Gly Pro Arg Ser Ala Ile Leu Phe Phe Cys Leu His Leu Ile
                165                 170                 175

Ser Tyr Ala His His Cys Ala Asn Ser Arg Leu Phe Ser
            180                 185
```

<210> 180
<211> 157
<212> PRT
<213> Homo sapiens

<400> 180

```
Val Ala Ile Cys Gln Val Pro Thr Asp Ile Pro Asn Ile Arg Leu Thr
1               5                   10                  15

Pro Ser Asn Gln His Pro Glu Phe Lys Val Cys Ile His Phe Leu Tyr
            20                  25                  30

Phe Tyr Cys Ile Arg Ile Ser Leu Asn Ser Ser Val Phe Ser Thr Phe
        35                  40                  45

Ile Tyr Gln Pro Tyr Leu Pro Phe Cys Asn Leu Leu Phe Ser Val Ser
    50                  55                  60

Ile Ile Phe Met Arg Leu Met His Ile Ala Val Tyr Ser Phe Leu Leu
65                  70                  75                  80
```

Leu Tyr Asn Ser Val Ile Pro Gly Met Gly Arg Gly Asn Trp Phe Gln
85 90 95

Asp Leu Cys Gly Leu Gln Asn Pro Ser Met Phe Lys Ser Leu Ile Asn
100 105 110

Glu Ala Val Leu Ala Tyr Asn Leu Cys Thr Phe Leu Arg Thr Leu Ser
115 120 125

Lys Cys Tyr Val Asn Gly Cys Phe Val Ile Cys Ile Ile Phe Ile Val
130 135 140

Met Phe Phe Leu Leu Phe Ser Pro Glu Phe Phe Phe Phe
145 150 155

<210> 181
<211> 219
<212> PRT
<213> Homo sapiens

<400> 181

Val Thr Leu Val Cys Tyr Ser Leu Met Val Arg Ser Leu Ile Lys Pro
1 5 10 15

Glu Glu Asn Leu Met Arg Thr Gly Asn Thr Ala Arg Ala Arg Ser Ile
20 25 30

Arg Thr Ile Leu Leu Val Cys Gly Leu Phe Thr Leu Cys Phe Val Pro
35 40 45

Phe His Ile Thr Arg Ser Phe Tyr Leu Thr Ile Cys Phe Leu Leu Ser
50 55 60

Gln Asp Cys Gln Leu Leu Met Ala Ala Ser Val Ala Tyr Lys Ile Trp
65 70 75 80

Arg Pro Leu Val Ser Val Ser Ser Cys Leu Asn Pro Val Leu Tyr Phe
85 90 95

Leu Ser Arg Gly Ala Lys Ile Glu Ser Gly Ser Ser Arg Asn Gly Arg
100 105 110

Thr Ser Trp Val Ser Ile Gln Leu Gly Gly Arg Asp Ala Gln Gly Thr
115 120 125

Asp Leu Gly Asn Ala Lys Val Lys Leu Gly Lys Asn Glu Leu Gln His
130 135 140

His Gln Gln Leu Val Cys Thr Gln Met Ser Ala Gly Gly Arg Gly Ala
145 150 155 160

Gln Asp Leu Leu Lys Val Ser Cys Cys Lys Gly His Phe Tyr Ile Asp
165 170 175

Val Lys Val Asn Lys Ser Met Glu Arg Ala Thr Lys Thr Lys Glu Asn
180 185 190

Phe Leu Lys Glu Ser His Trp Ser Leu Val Ile Gln Val Ser Ala Gln
195 200 205

Met Ser Pro Leu Arg Asp His Ser Cys Pro Pro
210 215

<210> 182
<211> 181
<212> PRT
<213> Homo sapiens

<400> 182

```
Gln Gly Glu Gly Gly Thr Gly Tyr Lys Arg Ser Ala Ala Ala Ala Pro
1               5                   10                  15

Ala Glu Ser Arg Arg Ala Gln His Ser Cys Pro Leu Asp Pro Ala Asp
            20                  25                  30

Pro Ser Arg Ala Pro Ser Val Pro Gln Ala Gln Pro Pro Gly Gly Arg
        35                  40                  45

Ala Glu Gly Ser Pro Gly Arg Cys Gln Gly Ala Ile Leu Glu Gly Gly
    50                  55                  60

Arg Glu Glu Glu Val Arg Ala Ala Met His Thr Val Ala Thr Ser Gly
65                  70                  75                  80

Pro Asn Ala Ser Trp Gly Ala Pro Ala Asn Ala Ser Gly Cys Pro Gly
                85                  90                  95

Cys Gly Ala Asn Ala Ser Asp Gly Pro Val Pro Ser Pro Arg Ala Val
            100                 105                 110

Asp Ala Trp Leu Val Pro Leu Phe Phe Ala Ala Leu Met Leu Leu Gly
        115                 120                 125

Leu Val Gly Asn Ser Leu Val Ile Tyr Val Ile Cys Arg His Lys Pro
    130                 135                 140

Met Arg Thr Val Thr Asn Phe Tyr Ile Gly Glu Cys Gly Pro Leu Arg
145                 150                 155                 160

Arg Thr Cys Cys Arg Pro Gly Gly Leu Arg Gly Pro Ser Gly Leu Gly
                165                 170                 175

Arg Pro Leu Ala Thr
            180
```

<210> 183
<211> 227
<212> PRT
<213> Homo sapiens

<400> 183

```
Ile Ile Leu Gln Asp Asn Leu Lys Gln Tyr Leu Val His Ile Asn His
1               5                   10                  15

Phe Ile Ser Ala Gly Leu Leu Ser Phe Glu Asn Tyr Phe Tyr His Leu
            20                  25                  30

Leu Leu Ala Thr Val Asn Leu Ser Asn Leu Val Ser His His Ser Leu
        35                  40                  45

Ile Pro Cys Ser Ala Leu Val Thr Met Asn Leu Ser Leu Leu Leu Lys
    50                  55                  60

Tyr Ala Ile Tyr His Val Phe Phe Phe Pro Phe Ser Leu Pro Glu Ala
65                  70                  75                  80
```

His Thr Pro Ser Leu Gly Trp Leu Lys Ser His Asn Leu Thr Phe Gly
85 90 95

Leu Thr Phe Tyr Asn Ser Leu Tyr Gln Pro Gln Asn Met Ala Trp Val
100 105 110

Met Leu Ala Leu Thr Val Leu Asp Phe Ser Asp Pro Ser Leu Leu Ile
115 120 125

Tyr Gln Pro Leu Ser Arg Ser Phe Gly Thr Tyr Ser Asp Phe His Thr
130 135 140

Pro Glu Leu Phe Ala Ile Leu Phe Ile Trp Lys Ser Tyr Trp Val Ile
145 150 155 160

Phe Leu Phe Lys Tyr Asn Leu Ile Ile Thr Pro Leu Val Tyr Leu Ala
165 170 175

Leu Ser Cys Ser Leu Tyr Phe Pro Cys Pro His Leu Asn Ser Leu Thr
180 185 190

Gly Glu Ile Asn Tyr Arg Tyr Thr Lys Gly Pro Asp Ser Lys Arg Asn
195 200 205

Ile Gly Lys Ile Ser Ser Pro Ser Gln Pro Gly Tyr Gln Ile Lys Asp
210 215 220

Arg Arg Leu
225

<210> 184
<211> 191
<212> PRT
<213> Homo sapiens

<400> 184

Pro Pro Thr Asp Ile Ser Val Cys Cys Ser Asp Gln Val Leu Gly His
1 5 10 15

His Gln Cys Pro Val Val Met Gly His Leu Lys Leu Tyr Leu Tyr Pro
20 25 30

Ser Ala Leu Leu Leu Asp Leu Leu His His Leu Leu His Met Asp Leu
35 40 45

Leu His Phe Gly Cys Val Val His His Leu His Thr Leu Pro Asn Lys
50 55 60

Asn Ile Gln Lys Pro Ser Ser Gln His His Cys Pro Gly His His Ser
65 70 75 80

Ser Leu Phe Phe Leu Asn Pro Ser Leu His Glu Arg Gln Arg Arg Leu
85 90 95

Thr Gly Ser Pro Leu Leu Val Asn His Met Lys Ile Lys His Ala Tyr
100 105 110

Ser Val Leu Val Gln Gln Glu Ile Tyr Phe Gln Thr Arg Lys Ala Thr
115 120 125

Glu Thr Leu Gly Ile Ile Leu Gly Ala Phe Ile Ile Cys Trp Leu Pro
130 135 140

Leu Phe Ile Val Ser Leu Pro Ala Lys Ile Pro Pro Tyr Asp Ile Phe

145 150 155 160

Ile Leu Leu Ser Phe Phe Phe Phe Phe Phe Leu Ile Pro Ser Leu Thr
165 170 175

Leu Val Ser Gln Ala Arg Met Gln Trp Tyr Asn Leu Ser Ser Leu
180 185 190

<210> 185
<211> 76
<212> PRT
<213> Homo sapiens

<400> 185

Ile Leu Pro Ala His Leu Ile Pro Leu Gly Lys Leu Trp Cys Cys Leu
1 5 10 15

Ser Arg Thr Glu Ala Glu Gly Trp Leu Ser Pro Thr Gly Ser Tyr Ser
20 25 30

Leu Asn Ser Ala Ser Ser Pro Arg Leu Gly Glu Thr Thr Trp Gly His
35 40 45

Arg Val Phe Ala Arg Cys His Phe Ala Phe Gln Thr Arg Ser Trp Ser
50 55 60

Ser Gly Phe Arg Leu Gly Leu Trp Asn Ser Gly Ala
65 70 75

<210> 186
<211> 99
<212> PRT
<213> Homo sapiens

<400> 186

Cys Arg Ala His His Ser Leu Thr Ser Phe Val Ser Trp Phe Arg Tyr
1 5 10 15

Asp Leu Pro Tyr Pro Asp His Ser Ile Asn Cys Lys Leu Pro Val His
20 25 30

Ser Ser Leu Ser Tyr Asn Thr Phe Pro Phe Ser Gln Arg Tyr Cys His
35 40 45

Phe Val Ser Tyr Tyr Ile Thr Tyr Tyr Val Tyr Cys Leu Leu Arg Ile
50 55 60

Leu Cys Ser Leu Met Tyr Leu Lys Tyr Leu Gly Gln Cys Ser Val His
65 70 75 80

Val Thr Gly Val Gln Gln Arg Leu Leu Asn Glu Ile Phe Asp Asn Cys
85 90 95

Asp Arg Tyr

<210> 187
<211> 194
<212> PRT
<213> Homo sapiens

<400> 187

Ala Glu Gln Val Leu Val Ile Phe Ala Glu Gln Val Leu Asn Glu Cys
1 5 10 15

Met Asn Lys Cys Met Asn Val Glu Met Lys Gly Asp Ala Asp Gly Asp
20 25 30

Asp Ala Asp Gly Asp Asp Asp Ala Asp Gly Asp Asp Ala Asp Gly Asp
35 40 45

Asp Ala Asp Gly Glu Gln Trp Pro Cys Arg Val Phe Ala Asp Leu Gly
50 55 60

Leu Ala Ser Gly Cys Gly Gly Ser Ala Ser Gln Gly Phe Glu Phe His
65 70 75 80

Leu Gln Cys Leu Pro Ala Met Pro Pro Trp Val Thr Phe Ile Leu Leu
85 90 95

Pro Gly Lys Trp Gly Cys Trp Gln Pro Leu Pro Pro Gly Ile Thr Asp
100 105 110

Thr Ala Trp Ser Gly Cys Asp Pro Phe Gly Tyr Arg Arg Gly Trp Trp
115 120 125

Thr Ser Gln Val Gly Arg Ser Ser Leu Asp Glu Arg Pro Arg Thr Ile
130 135 140

His Arg Arg Ala Gln Glu Ser Leu Leu Ser Pro Ser Asn Ser Thr Glu
145 150 155 160

Pro Ala Val Asn Cys Trp Leu Leu Pro Val Thr Phe Pro Cys Pro Tyr
165 170 175

Phe His Ser Leu Glu Ala Ala Arg Thr Thr Ala Gly Trp Pro Trp Pro
180 185 190

Leu Pro

<210> 188
<211> 178
<212> PRT
<213> Homo sapiens

<400> 188

Ser Phe Ser Leu Gly Asn Phe Val Val Ala Ser Leu Tyr Ser Cys Cys
1 5 10 15

Phe Asn Asn Phe Val Leu Phe His Ser Phe Thr Val Thr Val Cys Val
20 25 30

Asp Ser Phe Ser Ser Ser Val Lys Ile Met Ser Pro Glu Ser Ser Phe
35 40 45

Ile Thr Leu Asp Arg Thr Arg Thr Leu Ser Ile Lys Ser Met Leu Phe
50 55 60

Val Ile Thr Glu Gln Phe Ser Ala Val Ile Ser Leu Ile Val Thr Phe
65 70 75 80

Leu Phe Ile Pro Phe Ser Leu Ser Lys Met Pro Leu Phe Val Tyr Trp
85 90 95

Ser His Arg Ser Glu Ile Cys Glu Phe Ala Ile His Val Ser Tyr Leu

```
            100                 105                 110

Phe Ala Asn Gly Phe His Val Ser Lys Ser Leu Phe Ser Ile Val Arg
        115                 120                 125

Tyr Tyr Leu Tyr Cys Phe Val Gln Asn Ile Asn Leu Val Leu Phe Ile
    130                 135                 140

Asp Tyr Ser Leu Val Leu Leu Leu Asn Phe Ile Gln Glu Cys Val Phe
145                 150                 155                 160

Leu Ser Asp Tyr Phe Phe Leu Pro Asn Cys Ile Phe Leu Arg Gly Leu
                165                 170                 175

Ile Ile


<210>  189
<211>  76
<212>  PRT
<213>  Homo sapiens

<400>  189

Pro Arg Glu Ala Lys Arg Leu Asp Ile His Ala Pro Leu Leu Ser Leu
1               5                   10                  15

Pro Asp Cys His Leu Leu Met Ala Ala Ser Val Ala Tyr Lys Ile Trp
            20                  25                  30

Arg Pro Leu Gly Ser Val Ser Asn Cys Leu Asn Pro Leu Leu Tyr Phe
        35                  40                  45

Leu Ser Arg Gly Ala Lys Phe Glu Ser Gly Ser Ser Arg Asn Gly Arg
    50                  55                  60

Thr Ser Trp Val Ser Ile Gln Leu Gly Gly Arg Asp
65                  70                  75

<210>  190
<211>  189
<212>  PRT
<213>  Homo sapiens

<400>  190

Ser Leu Val Ile Leu Val Cys Tyr Ser Leu Met Val Arg Ser Leu Ile
1               5                   10                  15

Lys Pro Glu Glu Pro His Glu Val Gln Ala Thr Gln Pro Glu Pro Gly
            20                  25                  30

Pro Ser Gly Thr Ile Leu Leu Val Cys Gly Leu Phe Thr Leu Cys Phe
        35                  40                  45

Val Pro Phe His Ile Thr Arg Ser Phe Tyr Leu Thr Ile Cys Phe Leu
    50                  55                  60

Leu Ser Gln Asp Cys Gln Leu Leu Met Ala Ala Ser Val Ala Tyr Lys
65                  70                  75                  80

Ile Trp Arg Pro Leu Val Ser Val Ser Ser Cys Leu Asn Pro Val Leu
                85                  90                  95

Tyr Phe Leu Ser Arg Gly Ala Lys Ile Glu Ser Gly Ser Ser Arg Asn
```

100 105 110

Gly Arg Thr Ser Trp Val Ser Ile Gln Leu Gly Gly Arg Asp Ala Gln
115 120 125

Gly Thr Asp Leu Gly Asn Ala Lys Val Lys Leu Gly Lys Asn Glu Leu
130 135 140

Gln His His Gln Gln Leu Val Cys Thr Gln Met Ser Ala Gly Gly Arg
145 150 155 160

Gly Ala Gln Asp Leu Leu Lys Val Ser Cys Cys Lys Gly His Phe Tyr
165 170 175

Ile Asp Val Lys Val Asn Lys Ser Met Glu Arg Ala Thr
180 185

<210> 191
<211> 208
<212> PRT
<213> Homo sapiens

<400> 191

Ser His Ile Ser Pro Gly Thr Gly Cys Leu Ser Leu Pro Ala Ile Val
1 5 10 15

Trp Ala Leu Ala Gly Ser Ser Pro Trp Glu Met Trp Ala Arg His Ser
20 25 30

Asp Arg Ser Gln Ser Ala Gly Ala Gly Ala Phe Gly Leu Ser Ser Pro
35 40 45

Met Glu Val Ser Glu Pro His Ser His Ser Tyr Arg Arg His Gln Asn
50 55 60

Ser Leu Tyr Val Glu Pro His Lys Val Glu Thr Val Asn Ser Cys Arg
65 70 75 80

Asn Leu Leu Trp Asn Thr Thr Val Phe Glu Ser Gly Ser Asp Leu Thr
85 90 95

Ser Ser Val Thr Leu Gly Lys Leu Leu Leu Pro Trp Thr Pro Thr Thr
100 105 110

His Leu Asp Val Gly Asn Asn Asp Thr Glu Phe Ile Gly Leu Arg Leu
115 120 125

His Leu Met Gly Thr Leu Glu Gln Cys Gln Thr Gln Thr Thr Asn Ala
130 135 140

Gln Lys Leu Val Phe Ile Ile Ala Phe His Phe Asn Cys Gly Leu Leu
145 150 155 160

Gly Leu Asn Cys Val Pro Ser Lys Arg Tyr Ile Gly Val Leu Thr Leu
165 170 175

Ser Thr Ser Glu Cys Asp Cys Thr Trp Arg Leu Gly Leu Tyr Arg Asp
180 185 190

Asn Arg Val Lys Met Glu Leu Gln Gly Trp Ser Leu Ile Gln Cys Asp
195 200 205

<210> 192
<211> 211

<212> PRT
<213> Homo sapiens

<400> 192

Ile Leu Ser Ser Ser Leu Cys Leu Arg Pro Pro Ser Pro Glu Pro Ser
1 5 10 15

Glu Leu Ser Ala Ser Ser Leu Phe Ala Pro Pro Cys Cys Arg His Arg
20 25 30

Arg Phe Gly Ser Val Pro Ala Glu Val Gly Lys Asp Thr Trp Asn Ser
35 40 45

Gly Arg Pro Leu Cys Ser Pro Leu Ala Arg Ser Lys Ala Val Lys Asp
50 55 60

Thr Ala Ser Pro Gly Ser Cys Ser Ser Leu Asn Pro Thr Val Asp Leu
65 70 75 80

Val Gly Arg Leu Arg Ala Gln Ile Cys Arg Cys Ser Ile Val Ser Ser
85 90 95

Val Ser Cys Pro Leu Leu Pro Pro Gly Val Asp Ser Cys Thr Val His
100 105 110

Pro Thr Pro Ala Phe Pro Ser Phe Leu Ile Ser Pro Val Ile Phe Pro
115 120 125

Val Ala Leu Leu Cys Trp Cys Pro Val Arg Ser Cys Gly His Lys Arg
130 135 140

Leu His Gly Pro His Pro Gln Leu Gly Glu Ser Ser Pro Ser Trp Val
145 150 155 160

Leu Trp Thr Val Lys Lys Asp Gly His Val Gly Ser Val Glu His Glu
165 170 175

Val Val Gln Asp Leu Gly Gly His Arg Ser Cys Leu Pro Ala Ser Arg
180 185 190

Ala Leu Pro Pro Phe Gly Ser Leu Leu His Leu Gly Lys Arg Phe Val
195 200 205

Pro Thr Pro
210

<210> 193
<211> 208
<212> PRT
<213> Homo sapiens

<400> 193

Asn Met Ser Tyr Ser Ser Arg Val Asn Ser Leu Leu Leu Phe Ser Phe
1 5 10 15

Asn Phe Ser Tyr Ile Ile Phe His Ile Asn Phe Arg Ile Ser Leu Val
20 25 30

Trp Gly Val Ile Gln Val Asn Leu Ile Lys Phe Gly Glu Gly Phe Thr
35 40 45

Ile His Leu Ile Asn Phe Gly Arg Val Val Met Leu Met Phe Ser His
50 55 60

```
Tyr Ile Leu Lys Cys Asp Ile Ser Phe His Leu Phe Val Leu Asp Gln
65                  70                  75                  80

Ala Leu Val Ala Ser Ser Glu Asn Leu Leu Asn Ser Arg Asn Asn Phe
                85                  90                  95

Phe His Leu Leu Thr His Phe Leu Thr Ile Cys Phe Leu Pro Leu Val
            100                 105                 110

Leu Cys Leu Val Asn Tyr Phe Leu Leu Ile Ser Pro Leu Gln Ile Leu
        115                 120                 125

Tyr Ala Ile Arg Lys Gly Val Thr Asp Leu Val Ile Glu Thr Gln Tyr
    130                 135                 140

Thr Phe Val Gly Met Met Lys Ala Leu Gly Ile Phe Ser Tyr Tyr Val
145                 150                 155                 160

His Leu Ile Ile Leu Lys Leu Ser Ser Tyr Val Glu Pro Ile His Lys
                165                 170                 175

Ser Arg Ser Phe Asp Phe Lys Ser Cys Ile Phe Pro Tyr Phe Gln Tyr
            180                 185                 190

Leu Ile Gly Glu Val Thr Cys Asn Ala Ile Val Leu Gln Phe Tyr Ile
        195                 200                 205
```

<210> 194
<211> 213
<212> PRT
<213> Homo sapiens

<400> 194

```
Met Thr Gly Asn Ala Val Val Leu Trp Leu Leu Gly Phe Arg Met Arg
1               5                   10                  15

Arg Asn Ala Phe Ser Ile Tyr Ile Phe Asn Leu Ser Met Ala Asp Phe
            20                  25                  30

Leu Phe Leu Arg Ser His Ile Ile Arg Phe Pro Leu Ser Leu Ile Asn
        35                  40                  45

Ile Leu His Pro Ile Phe Lys Ile Leu Ser Pro Val Met Met Phe Ser
    50                  55                  60

Tyr Leu Ala Ser Leu Ser Phe Leu Ser Ala Met Ser Thr Glu Arg Cys
65                  70                  75                  80

Leu Tyr Val Leu Trp Pro Ile Trp Arg Cys Arg Pro Arg Pro Tyr Thr
                85                  90                  95

Cys Gln Arg Ser Cys Val Ser Cys Ser Gly Pro Cys Leu Cys Cys Gly
            100                 105                 110

Ala Ser Trp Ser Gly Val Ser Val Thr Ser Cys Leu Val Val Leu Ile
        115                 120                 125

Leu Phe Gly Val Lys His Gln Ile Ser Ser Gly Gly Phe Phe Tyr Val
    130                 135                 140

Trp Leu Ser Val Val Pro Ala Trp Ser Cys Trp Ser Gly Ser Phe Val
145                 150                 155                 160
```

Gly Pro Gly Arg Cys His Pro Gly Cys Thr Pro Ser Cys Ser Arg Trp
165 170 175

Ser Ser Ser Phe Cys Gly Leu Pro Phe Gly Ile Arg Phe Phe Leu Phe
180 185 190

Ser Trp Asn His Val Asp Leu Glu Val Leu Tyr Cys His Val His Leu
195 200 205

Val Ser Ile Phe Leu
210

<210> 195
<211> 190
<212> PRT
<213> Homo sapiens

<400> 195

His Thr His Thr His Thr His Thr His Thr His Thr His Thr Arg Thr
1 5 10 15

His Pro Ile Asn Gly Phe Pro Gly Gly Arg Ala Ser Val Pro Leu Thr
20 25 30

Ala Gly Pro Pro Gly Pro Ala Lys Gly Ala Lys Ser His Ser Asp Ile
35 40 45

Asn Ser Trp Phe Gln Ser Asn Lys Gln Ser Asn Val Arg Lys Val Ile
50 55 60

Arg Leu Lys Gly Phe Glu Gly Lys Ser His Gln Lys Val Lys Leu Asp
65 70 75 80

Pro Thr Ser Thr Ser Trp Met Ser Tyr Leu Ile Ser Leu Ala Ser Val
85 90 95

Phe Ser Pro Ile Lys Lys Pro Glu Asp Leu Pro His Gln Ala Val Leu
100 105 110

Lys Leu Asn Glu Leu Ile Pro Val Gln Ala Glu Asn Ser Ile Tyr Ser
115 120 125

Ile Ser Gln Leu Leu Leu Leu Leu Leu Leu Leu Cys Thr Trp Leu Ser
130 135 140

Leu Phe Ser Phe Ile Asn Tyr Tyr Ser Leu His Leu Phe Ala Ala Thr
145 150 155 160

Trp Ser Ser Trp Asn Pro Phe Thr Ala Tyr Ser Arg Glu Thr Gly Glu
165 170 175

Gly Arg Cys His Leu His Ser His Trp Asp Ala Pro Ala Pro
180 185 190

<210> 196
<211> 138
<212> PRT
<213> Homo sapiens

<400> 196

Glu Asn Leu Phe Phe Lys Gly Lys Phe Val Ser Asn Thr Leu Pro His
1 5 10 15

Ser Phe Ile Arg Gln Cys Phe Leu Cys His Phe Ser Ala Arg Ile Leu
20 25 30

Leu Leu Gly Ile Glu Phe Thr Val His Ser Ser Val Leu Ser Val Leu
35 40 45

Gln Lys Tyr Tyr Leu Phe Pro Ser Asn Leu His Gly Phe Arg Trp Lys
50 55 60

Ile Cys Cys Gly Leu His Tyr Cys Phe Ser Val Arg Asn Val Pro Phe
65 70 75 80

Phe Leu Cys Leu Leu Ser Arg Phe Leu Ile Phe Phe Phe His Phe Gln
85 90 95

Lys Leu Asn Val Phe Gly Cys Ile Leu Phe Arg Val Cys Ser Cys Phe
100 105 110

Leu Glu Tyr Leu Gly Leu Cys Ser Ser Ile Leu Ile Trp Glu Gly Ser
115 120 125

His Tyr Phe Leu Ile Val Phe Ser His Ile
130 135

<210> 197
<211> 175
<212> PRT
<213> Homo sapiens

<400> 197

Ser Asp Ser Pro Ile Tyr Asn Leu Cys His Thr Asn Arg Leu Asn Pro
1 5 10 15

His Cys Glu Phe His Thr Cys Val Asp Val Ser Thr Ser Arg Asp Gly
20 25 30

Cys Ile Phe Phe Ile Phe Leu His Thr Phe Leu Glu Tyr Phe Ile Ser
35 40 45

Met Val Leu Gln Ile Leu Leu Pro Thr Tyr Cys Gly Phe Lys Ala Met
50 55 60

Glu Lys Thr Lys Ser His Arg Ser Lys Tyr Cys Arg Lys Gln Asn Ser
65 70 75 80

Trp Val Asp Leu Ile Phe Leu Tyr Lys Asn Tyr Gly Tyr Gly Tyr Met
85 90 95

Tyr Leu Cys Met Ser Val Ala Lys Ile Asn Lys Met Asn Thr Phe Asn
100 105 110

Leu Arg Val Pro Ile Ile Gln Phe Thr Ser Phe Cys Pro Thr Thr Leu
115 120 125

Glu Ala Lys Thr Leu Val Glu Thr Leu Met Cys Phe Thr Ser Asn Ser
130 135 140

Ser Leu Ala Leu Asn Ile Pro Leu Phe Val His Pro Leu Ser Asp Ala
145 150 155 160

Ile Leu Leu Val Lys Gln Gln Thr Ser Thr His Arg Lys Leu Glu
165 170 175

<210> 198

<211> 177
<212> PRT
<213> Homo sapiens

<400> 198

Ser Arg Lys Gly Arg His Trp Arg Gly Cys Leu Leu Thr Leu Leu Met
1 5 10 15

Leu Val Ala Val Val Val Cys Phe Ser Pro Tyr His Leu Asn Ile Lys
20 25 30

Gln Phe Met Ala Arg Gly Met Leu His Leu Pro Ser Cys Ala Glu Arg
35 40 45

Arg Ala Phe Leu Leu Ser Leu Gln Ala Thr Val Ala Leu Met Asn Met
50 55 60

Asn Cys Gly Ile Thr Pro Ser Phe Thr Ser Leu His Pro Pro Ile Thr
65 70 75 80

Gly Asn Gly Ser Trp Ala Phe Ser Ser Lys Gly Leu Pro Pro Pro Pro
85 90 95

Pro Pro Pro Pro Pro Gln Glu Lys Leu Leu Gln Lys His Gln Val Ser
100 105 110

Pro Arg Pro Glu Val Leu Cys Ser Arg Ser Thr Trp Ser Asn Val Ser
115 120 125

Phe Ala Leu Leu Tyr Leu Gly Arg Gly Pro Ala Leu Gly Tyr Ser Tyr
130 135 140

Asn Leu Gly Lys Arg Phe Phe Lys Glu Lys Asn Thr Glu Glu Ile Gln
145 150 155 160

Asn Ala Gly Arg Gly Gly Ser Arg Leu Ser Pro His Phe Gly Arg Pro
165 170 175

Arg

<210> 199
<211> 202
<212> PRT
<213> Homo sapiens

<400> 199

Val Tyr Glu Cys Tyr Ile Phe Gly His Cys Trp Asp Val Ala Ser His
1 5 10 15

His Leu Thr Ser Leu Asn Leu Ser Gly Leu Thr Cys Glu Met Gly Ala
20 25 30

Leu Thr Phe Thr Cys Leu Gln Ala Cys Ser Gln Ile Arg Cys His Leu
35 40 45

Lys Asp Phe Ser Ser Pro Gly Asp Phe Lys Arg Leu Leu Arg Gly His
50 55 60

Phe Phe Ser Gly Cys Gly Arg Ser Met Ile Arg Val Ile Arg Met Gly
65 70 75 80

Leu Leu Glu Glu Arg Gly Gly Gln Arg Leu Leu Phe His Phe Met Ala

85 90 95

Pro Ser Gly Gln Arg Thr Asp Ser Ala Thr Ala Ala Thr Arg Ala Leu
100 105 110

Pro Gly Leu Trp Ser Gln Leu Ser Gln Gln Glu Phe Gln Lys Ala Lys
115 120 125

Gly Ser Glu Leu His Pro Ser Phe Leu Ala Asp Cys His Pro Ala Ser
130 135 140

Ser His Ser Pro Gln Gly Tyr Val Met Leu Ala Leu Lys Ala Ser Leu
145 150 155 160

Gly Arg Gly Cys Ile Cys His Pro Leu Pro Cys Lys Ile Phe Glu Val
165 170 175

Gln Arg Ala Leu Gln Ala Glu Pro His Pro Leu Leu His Ser Pro Ser
180 185 190

Val Gly Met His Ser Pro Ser Val Gly Met
195 200

<210> 200
<211> 175
<212> PRT
<213> Homo sapiens

<400> 200

Leu Pro Pro Pro Pro Ile Leu Val Pro Thr Val Val Thr Glu Glu Ile
1 5 10 15

Phe Ser Ser Ser Thr Ala Thr Leu Lys Gly Pro Ser Val Pro Phe Gly
20 25 30

Gly Leu Gly Ile Asp Leu Pro His Arg Ser Ser Leu Ala Pro Met His
35 40 45

Thr Phe Arg Asp Leu Arg Thr Gly Pro Leu Cys Leu Pro Leu Ser Leu
50 55 60

Leu Val Arg Lys Asp Trp Pro Ala Cys Leu His Pro Gln Gln Ser Ile
65 70 75 80

Ala Thr Ala Pro Ser Cys Ala Thr Glu Glu Leu Thr Asp Thr Thr His
85 90 95

Thr Val Tyr Ser Arg Arg Asn Pro Met Gly Pro Ile Ile Leu Cys Pro
100 105 110

Pro Trp Ile Lys Thr Lys Val Leu Tyr Ala Thr Asn Thr Thr Ala Ile
115 120 125

Ser Thr Gly Lys Ser Leu Ser Leu Gln Lys Pro Ile Gln Lys Pro Arg
130 135 140

Arg Ser Asn Cys His Thr Lys Tyr Thr Asp Thr Asn Leu Arg Thr Glu
145 150 155 160

Thr Glu Asn Lys Glu Thr Trp His Phe Leu Lys Glu His Asn Asn
165 170 175

<210> 201
<211> 178

<212> PRT
<213> Homo sapiens

<400> 201

Leu Gly Phe Leu Leu Thr Asp Val Gln Ser Val Phe Gly Tyr Leu Gln
1 5 10 15

His Glu Thr His Tyr Cys Ser Ala Thr Ile Gly Arg His Trp Pro Ala
20 25 30

His Pro Leu Met Arg Cys Trp Asn Pro Phe Phe Ile Leu Lys Tyr Leu
35 40 45

Ile Asp Lys Asn Cys Val Cys Ser Arg Cys Asp Val Met Leu Arg Ser
50 55 60

Arg Tyr Ile Gln Val Tyr Leu Pro Gln Ser Asn Leu Thr Asn Leu Ser
65 70 75 80

Pro Pro Met Ile Thr Ile Met Leu Arg Gly Gly Ser Glu Asp Thr Lys
85 90 95

Asp Leu Leu Ser Tyr Gln Ile Ser Ser Gln Gln Tyr Ser Ile Ile Asn
100 105 110

Thr Val Thr Met Leu Cys Ile Arg Ser Pro Glu His Val Thr Glu Gly
115 120 125

Leu Tyr Leu Leu Thr Asn Ile Ser Pro Ala Leu His Glu Trp Met Val
130 135 140

Ser Ile Phe Gln Thr His Ser Glu Asp Phe Ala Trp Leu Ala Thr Ser
145 150 155 160

Ile Ser Pro Glu Lys Val Gln Lys Ser Arg Pro Ser His Arg Asn Ser
165 170 175

Asp Ala

<210> 202
<211> 196
<212> PRT
<213> Homo sapiens

<400> 202

Tyr Gly Ala Leu Tyr Lys Tyr Lys Gln Gln Ser Leu Thr Phe Leu Ser
1 5 10 15

Leu Gln Leu Leu Thr Leu Ala Gly Ser Arg Ile Lys Met Pro Asn Ser
20 25 30

Thr Gln Lys Pro Trp Pro Val Ser Leu Pro Lys Met Glu Phe Arg Leu
35 40 45

Thr Ala Gly Asn Arg Asn Cys Ser Phe Lys Ala Ile Ala Trp Ala Met
50 55 60

Val Pro Ile Phe Val Asn Ile Gly Phe Cys Leu Asn Ser Val Ser Arg
65 70 75 80

Val Asp Tyr Ile Ile Cys Lys Val Cys Lys Met Lys Val Trp Gly Ser
85 90 95

Ser Ser Lys Tyr Lys Gln Lys Val Leu Leu Ser Val Ser Lys Tyr Lys
100 105 110

Met Phe Pro Leu Ser Val Ile Tyr Phe Ser Thr Cys Tyr Val Phe Gln
115 120 125

Phe Val Cys Phe Val Phe Pro Leu Leu Phe Tyr Val Leu Leu Cys Lys
130 135 140

Lys Ile Lys Asn Leu Asn Tyr His Asn Lys Phe Ser His Ser Phe Leu
145 150 155 160

Cys Cys Ala Val Ser Ile Asn Ala Asn Ile Lys Ala Phe Asn Leu Tyr
165 170 175

Ile Glu Ser Gln Lys Leu His Asn Thr Tyr Phe Ile Val Cys Thr Cys
180 185 190

Met Tyr Ile Leu
195

<210> 203
<211> 212
<212> PRT
<213> Homo sapiens

<400> 203

Ser Gly Val Ile Asn Leu Leu Tyr Ile Cys Val Tyr Val Cys Ile Phe
1 5 10 15

Leu Pro Asn Arg Cys Asn Thr Lys Tyr Ser His Gly Val Ile Thr Phe
20 25 30

Ser Gln Leu Thr Leu His Pro Tyr Ile Ile Glu Glu Arg Ser Thr Ser
35 40 45

Ile Leu Phe Leu Leu Val Ile Ala Leu Met Ser Glu Tyr Lys Leu Asp
50 55 60

Ser Ser Val Ala Asn Asn Thr Arg Gln Ser Lys Asp Phe Ser Cys Cys
65 70 75 80

Arg His Ile Phe Leu Ile Tyr Trp Lys His Lys Cys Val Pro Pro Asn
85 90 95

Phe Ile Val Asp Arg Asn Met Lys Asn Phe Ile Lys Leu Lys Thr Gly
100 105 110

Ser Leu Pro Asp Leu Pro Val Ile Leu Pro Thr Leu Gln Ile His Pro
115 120 125

Ile Val Pro Ala Ser Phe Thr Met Lys Lys Tyr Glu Thr Cys Leu Thr
130 135 140

Trp Ser Leu Cys Leu Arg Glu Thr Cys Val Cys Leu Trp Asn Thr Leu
145 150 155 160

Thr Lys Ile Pro Ala Leu Val Asp Lys Thr Gly Phe Gln Ser Ser Leu
165 170 175

Asn Ser His Phe Val Leu Asn Lys Val Val Ser Lys Thr Arg Cys Ser
180 185 190

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Lys Tyr Tyr Cys Ser Asp Ala Ile Ser Lys Thr Val Leu Ile Pro Cys
        195                 200                 205

Gly Arg Glu Asn
    210

<210>  204
<211>  172
<212>  PRT
<213>  Homo sapiens

<400>  204

Asn Lys Ile Val Phe Ile Phe Ser His Asp Cys Leu Trp Arg Lys Ile
1               5                   10                  15

Ser Lys Asn Leu Pro Lys Thr Asn Ala Ile Leu Ser Arg Val Lys Glu
            20                  25                  30

Thr Arg Ser Ser Leu Phe Cys Thr Leu Tyr Phe Cys Ile Ser Val Leu
        35                  40                  45

Phe Leu Tyr Gly Ser Asn Asp Gln Leu Glu Ile Lys Ile Leu Lys Gln
    50                  55                  60

His Gln Lys His Lys Met Leu Ser Tyr Lys Ser Asn Lys Thr Tyr Thr
65                  70                  75                  80

Asp Ser Val Pro Lys Thr Val Asn Val Tyr Leu Lys Asn Gln Arg Arg
                85                  90                  95

Ala Glu Gln Arg Ala Thr Ser Cys Leu Leu Leu Glu Asn Ser Ile Glu
            100                 105                 110

Leu Arg Tyr Lys Phe Pro Gln Ser Asp Leu Asp Ala Thr Gln Phe His
        115                 120                 125

Ser Asn Pro Ser Arg His Phe Leu Leu Lys Ser Thr Ser Cys Phe Ile
    130                 135                 140

His Thr Lys Ile His Lys Asn Lys Lys Ala Lys Ile Leu Leu Lys Glu
145                 150                 155                 160

Asn Lys Phe Arg Arg Leu Leu Leu Ser Asp Phe Arg
                165                 170

<210>  205
<211>  313
<212>  PRT
<213>  Homo sapiens

<400>  205

Val Pro Lys Ile Phe Ser Phe Ser Ser Ser Phe Gln Asn Tyr Phe Leu
1               5                   10                  15

Ile Leu Val Lys His Thr Ser Ser Asn Ile Thr Tyr Tyr Leu Val Phe
            20                  25                  30

Thr Tyr Ile Thr His Ser Leu Asn Lys Phe Val Glu Met Ile Ile Leu
        35                  40                  45

Lys Ile Leu Val Phe Lys Phe Met Ser Ser Gln Lys Leu Leu Pro Arg
    50                  55                  60
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Ile Ser Ile Leu Asn Ile Trp Ile Asn Ile Leu Phe Tyr Thr Pro Tyr
65 70 75 80

Asn Ile Leu Leu Ala Ile Ile Ile Phe Phe Arg Ile Cys Ser Thr Ser
85 90 95

Asn Phe Phe Asp Phe Leu Ile Leu Lys Arg Ile Ile Tyr Ala Asn Gln
100 105 110

Gln Cys Lys Asp Phe Ser Trp Phe Thr Arg Val Lys Leu Phe Ser Arg
115 120 125

Met Val Gly Ser Phe Ala Tyr Ile Lys Leu Met Tyr Arg Ser Ala Ser
130 135 140

Ser His Ile Lys Val Gln Ser Leu Leu Lys Lys His Phe Ile Ser Asn
145 150 155 160

Gln Phe Val Phe Leu Tyr Thr Leu Lys Pro Phe Asn Cys Phe Tyr Phe
165 170 175

Ser Ile Leu Thr Ser Ile Ser Cys Tyr Ser Gln Trp Pro Ala Ser Ser
180 185 190

Leu Ala Ile Arg Gln Leu Phe Val Tyr Leu Ala Lys Tyr Ile His Ala
195 200 205

Leu Lys Ile Pro Phe Pro Asn Ile Tyr Tyr Asp Phe Phe Lys Gly Phe
210 215 220

Ser Phe Val Thr Met Thr Leu Lys Ala Lys Val Ser Arg Cys Cys Ile
225 230 235 240

Thr Val Gly Ser Thr Ile Met Tyr Gln Glu Gly Arg Glu Asn Gln Gly
245 250 255

Thr Phe Leu Trp Glu Tyr Pro Ile Ile Cys Gln Ile Tyr Ser Asn Ser
260 265 270

Leu Arg Thr Ile Thr Phe Val Phe Thr Val Phe Pro Met Gln Phe Leu
275 280 285

Arg Phe Ile Phe Lys Asn Phe Leu Gly Glu Met Asp Tyr Ser Leu Leu
290 295 300

Ser Ala Val Ile His Asn Phe Tyr Phe
305 310

<210> 206
<211> 318
<212> PRT
<213> Homo sapiens

<400> 206

Pro Phe Tyr Tyr Ser Met Leu Val Pro Thr Ser Gly Leu Ser Thr Cys
1 5 10 15

Cys Ser Phe Cys Leu Glu Ser Ser Ser Pro Asp Leu Leu Arg Phe Pro
20 25 30

Leu Ser Ile Arg Val Ser Ala Val Ile His Pro Gln Arg Arg Ser Pro
35 40 45

Asp Pro Val Lys Pro Pro Ile Pro Gln Ser Pro Tyr Val Ser Thr Ser

50 55 60

Leu Tyr Leu Ile Ser Gln His Leu Leu Ile Ser Leu Thr Leu His Tyr
65 70 75 80

Met Cys Cys Tyr Met Phe Val Ile Leu Ser Ser Gly Pro Cys Asn Val
85 90 95

Arg Met Ala Gln Tyr Lys Trp Gln Glu Gly Cys Arg Gly Val Asp Lys
100 105 110

Ala Glu Ser Gly Trp Gly Ser Trp Arg Asp Gly Gln Gly Pro Glu Leu
115 120 125

Arg Arg Trp Tyr Leu Gln Cys Ala Leu Asn Cys Pro Gly Met Ile Ile
130 135 140

Ser Ile Ala Ser Phe His Ser Gln Arg Cys Pro Gly Tyr Tyr Ser Cys
145 150 155 160

Ser Val Tyr Arg Ala Trp Ala Val Gly Ile Leu Phe Gln Met Gly Cys
165 170 175

Glu Ala Cys Gly Trp Phe Ala Gly Ser Asp Met Ile Leu Ala Phe Lys
180 185 190

Asp His Asp Gln Val Leu Glu Thr Leu Phe Trp Leu Leu Pro Thr Pro
195 200 205

Pro His Thr His Pro Thr Leu Leu His Cys Pro Phe Ser Leu Leu Trp
210 215 220

Gln Leu Phe Leu Phe Tyr Asn Leu Ile Leu Glu Phe Leu Gln Thr Ser
225 230 235 240

Gly Ser Gln Leu Gly Ala Ile Ser Pro Pro Arg Asp Ile Trp Tyr Phe
245 250 255

Ile Trp Arg Tyr Phe Trp Ser Gln Leu Glu Arg Val Leu Ala Ser Ser
260 265 270

Gly Arg Pro Gly Arg Leu Leu Thr Ile Leu Gln Ser Thr Glu Gln Pro
275 280 285

Tyr Thr Ile Lys Asn Asp Leu Thr Gln Asn Ala Ser Ser Pro Glu Val
290 295 300

Lys Lys Pro Cys Thr Arg Leu Ala Pro Ser Asn Arg Asn Ile
305 310 315

<210> 207
<211> 318
<212> PRT
<213> Homo sapiens

<400> 207

Ile Ser Pro Phe Tyr Tyr Ser Met Leu Val Pro Thr Ser Gly Leu Ser
1 5 10 15

Thr Cys Cys Ser Phe Cys Leu Glu Ser Ser Ser Pro Asp Leu Leu Arg
20 25 30

Phe Pro Leu Ser Ile Arg Val Ser Ala Val Ile His Pro Gln Arg Arg
35 40 45

Ser Pro Asp Pro Val Lys Pro Pro Ile Pro Gln Ser Pro Tyr Val Ser
50 55 60

Thr Ser Leu Tyr Leu Ile Ser Gln His Leu Leu Ile Ser Leu Thr Leu
65 70 75 80

His Tyr Met Cys Cys Tyr Met Phe Val Ile Leu Ser Ser Gly Pro Cys
85 90 95

Asn Val Arg Met Ala Gln Tyr Lys Trp Gln Glu Gly Cys Arg Gly Val
100 105 110

Asp Lys Ala Glu Ser Gly Trp Gly Ser Trp Arg Asp Gly Gln Gly Pro
115 120 125

Glu Leu Arg Arg Trp Tyr Leu Gln Cys Ala Leu Asn Cys Pro Gly Met
130 135 140

Ile Ile Ser Ile Ala Ser Phe His Ser Gln Arg Cys Pro Gly Tyr Tyr
145 150 155 160

Ser Cys Ser Val Tyr Arg Ala Trp Ala Val Gly Ile Leu Phe Gln Met
165 170 175

Gly Cys Glu Ala Cys Gly Trp Phe Ala Gly Ser Asp Met Ile Leu Ala
180 185 190

Phe Lys Asp His Asp Gln Val Leu Glu Thr Leu Phe Trp Leu Leu Pro
195 200 205

Thr Pro Pro His Thr His Pro Thr Leu Leu His Cys Pro Phe Ser Leu
210 215 220

Leu Trp Gln Leu Phe Leu Phe Tyr Asn Leu Ile Leu Glu Phe Leu Gln
225 230 235 240

Thr Ser Gly Ser Gln Leu Gly Ala Ile Ser Pro Pro Arg Asp Ile Trp
245 250 255

Tyr Phe Ile Trp Arg Tyr Phe Trp Ser Gln Leu Glu Arg Val Leu Ala
260 265 270

Ser Ser Gly Arg Pro Gly Arg Leu Leu Thr Ile Leu Gln Ser Thr Glu
275 280 285

Gln Pro Tyr Thr Ile Lys Asn Asp Leu Thr Gln Asn Ala Ser Ser Pro
290 295 300

Glu Val Lys Lys Pro Cys Thr Arg Leu Ala Pro Ser Asn Arg
305 310 315

<210> 208
<211> 320
<212> PRT
<213> Homo sapiens

<400> 208

Lys Leu Thr Leu Ala Ala Tyr Thr Leu Ile Gln Cys His Leu Pro Cys
1 5 10 15

Val Ile His Asn Ile Leu Tyr Glu Ser Tyr Phe Leu Cys Val Cys Val
20 25 30

Pro Phe Phe Glu Glu Tyr Asp Leu Ser Gln Phe Phe Cys Phe Ser Leu
35 40 45

Ser Pro Phe Asn Ile Ser Arg Ala Phe Val Val Val Thr Gly Glu Thr
50 55 60

Thr Tyr Thr Ser Phe Leu Leu Leu Phe Cys Tyr Leu Gln Phe Cys Met
65 70 75 80

Thr Leu Lys Gln Lys Asn Asn Tyr Leu Thr Ile Ser Phe Val Leu Tyr
85 90 95

Ser Gly Phe His Ile Gln Ser Pro Phe Ile Met Leu Leu Pro Leu Phe
100 105 110

Ser Ser Val Phe Glu Asp Gly Lys Ile His Gln His Pro Lys Tyr Gln
115 120 125

Pro Glu Arg Lys Lys Glu Ser Gly Trp Arg Gln Asp Ser Phe Gln Ser
130 135 140

Ile Ser Ser Thr Asp His Gly Ala Ala Ala Lys Arg His Ser Lys Arg
145 150 155 160

Val Glu Arg Gly Lys Thr Ser Ser Leu Arg Cys Leu Pro Phe Lys Phe
165 170 175

Thr Ile Ile Ile Arg Met Leu Leu Glu Glu Glu Gln Gly Gln Gly His
180 185 190

Phe Cys Asn Met Thr Gln Lys Asn Ile Asp Leu Lys Phe Asp Thr Tyr
195 200 205

Glu Leu Ser Lys Cys Arg Glu Lys Leu Pro Pro Cys Cys Thr Cys Met
210 215 220

Cys Ala Ile His Phe Ile Leu Ile Lys Val Cys Lys His Glu Met Gln
225 230 235 240

Gly Thr Asp His Leu Phe Met Arg Met Gln His Ser Ser Glu Lys Val
245 250 255

Tyr Leu Pro Lys Thr Glu Tyr Met Phe Ile Leu Lys Phe Phe Phe Leu
260 265 270

Phe Leu Phe Leu Ile Val Ile Lys Tyr Lys His Lys Phe Thr Ile Leu
275 280 285

Ile Ile Phe Lys Tyr Thr Val Gln Tyr Val His Ser His Tyr Cys Ala
290 295 300

Thr Asn Phe Gln Asn Ser Phe Tyr Leu Ala Lys Met Lys Leu Tyr Thr
305 310 315 320

<210> 209
<211> 315
<212> PRT
<213> Homo sapiens

<400> 209

Gln Pro Phe Ser Met His Ser Leu Glu Glu Lys Phe Phe Phe Phe Leu
1 5 10 15

Asn His Tyr Ser Ala Thr Ser Ile Ser Leu Glu Phe Leu Ser Ser Glu

20 25 30

Thr Leu Val Gln Val Ser Trp Gly Ile Arg Ile Val Cys Val Trp Ile
35 40 45

Thr Lys Tyr Tyr Arg Leu Arg Gly Glu Glu Thr Leu Trp Ser Phe Arg
50 55 60

Pro Thr Leu Ile Cys Leu Asp Leu Phe Cys Phe Lys Glu Ser His Leu
65 70 75 80

Gln Arg Thr Ala Ser Asp Ser Pro Cys Ser Val Phe Ser Gln Glu Cys
85 90 95

Ser Leu His Gln Pro Gln Glu Val Leu Gln Lys Glu Val Phe His Val
100 105 110

Gln Ile Thr Leu Arg Ser Asn Ser His His Ile Asp Phe Glu Tyr Ser
115 120 125

Cys Arg Lys Thr Cys Leu Tyr Gln Leu Gly Val Ser Pro Asn Leu Phe
130 135 140

Gly His Gly Asn Ser Phe Ser Lys Lys Thr Cys Phe Ser Ile Ser Phe
145 150 155 160

His Arg Lys Leu Thr Val Val Cys Val Phe Phe Gln Ile Ile His Ile
165 170 175

Tyr Ser Lys Leu Lys Leu His Trp Leu Phe Gly Phe Ile Asn Pro Leu
180 185 190

Thr Ser Val Leu Phe Phe Ser Thr Thr Cys Cys Leu Ala Thr Ser Ala
195 200 205

Cys Phe Val Trp Leu Asp Phe Leu Val Leu Ser Ile Gly Leu Arg Phe
210 215 220

Tyr Ile Leu Ser Cys Trp Asn His Pro Thr Ser Pro Ala Trp Leu Phe
225 230 235 240

Gly Ser Arg Leu Ser His Leu Val His Ser Ser Ala Val Asp Leu Tyr
245 250 255

Tyr Ser Leu Met Ser Ala Tyr Ser Leu His Leu Tyr Ser Phe Cys Leu
260 265 270

Glu Met Met Ser Arg Thr Gly Gln Gly Trp Tyr His Ser Ile Asn His
275 280 285

His Pro Leu Ile Leu Thr Val Asn Leu Pro Asn Lys Ile Phe Gln Lys
290 295 300

Arg Val Ser Asn Asn Pro Cys Leu Pro Leu Trp
305 310 315

<210> 210
<211> 327
<212> PRT
<213> Homo sapiens

<400> 210

Arg Val Pro Ser Leu Pro Gly Pro Pro Ala Thr Val Cys Pro Val Pro
1 5 10 15

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Ala Ser Glu Phe Ser Gln His Arg Lys Arg Gly Leu Arg Thr Ile Gln
            20                  25                  30

Pro Val His Ser Arg Glu Ser Leu Ser Val Ser Gln Arg Leu Met Gly
        35                  40                  45

Cys Leu Trp Cys Arg Val Thr Pro Ala Ser Pro Cys Gly Gly Cys Ala
    50                  55                  60

Gly Gly Ala Arg Pro Pro Pro Cys Ala Leu Ser Leu Ala Gln Gly Gln
65                  70                  75                  80

His Thr Ala His Pro Leu Phe Phe Leu Pro Phe Pro Leu Ala Gln Pro
                85                  90                  95

Leu Val Val Gly Val Thr Arg Gly Ala Glu Arg Ser Trp Arg Ser Arg
            100                 105                 110

Ala Cys Pro Gly Pro Val Arg Glu Gly Gly Arg Gly Gln Gln His Pro
        115                 120                 125

Trp Arg Arg Glu Asp Tyr Ile Ile Phe Ile Tyr His Met Pro Lys Ile
    130                 135                 140

Ala Leu Leu Arg Ala Phe Asp Ile His Pro Lys Ile Phe Lys His Tyr
145                 150                 155                 160

Gly Ser Met Ser Gly Cys Ile Ser Asn Met Lys Val Glu Ala Ser Cys
                165                 170                 175

Pro Ala Pro Ser Pro Leu Trp Glu Asn Phe Val His Val Leu Ser Gln
            180                 185                 190

Leu Phe Gly Lys Gly Gly Pro Ser His Cys Pro Leu Gly Gly Phe Asp
        195                 200                 205

Val His Cys Val Gly Arg Ser Leu Pro Ser Ile Leu Phe Tyr Phe Cys
    210                 215                 220

Arg Ile Ser Ala Gln Ser Gly Ser Ala Trp Gln Phe Ser Cys Ser Ala
225                 230                 235                 240

Arg Glu Val Leu Cys Pro Gly Leu Cys Asp Phe Arg Arg Arg Glu Gly
                245                 250                 255

Ser Cys Arg Pro Tyr Leu Gln Trp Leu Pro Pro Gly Ile Pro Val Cys
            260                 265                 270

Ser Leu Cys Thr Val Gln Arg Arg Ser Gly Ser Trp Trp Arg Asp Gly
        275                 280                 285

Asp Pro Arg Thr Met Ala Ser Thr Lys Ala Gly Gly Ala Cys Asp Arg
    290                 295                 300

Arg Trp Thr Met Thr Gln Val Pro Ala Arg Tyr Gly Ser Gly Leu Cys
305                 310                 315                 320

Arg Glu Gly Ala His Pro Gly
                325
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<210> 211
<211> 327
<212> PRT
<213> Homo sapiens

<400> 211

Cys Gln Phe Gly Ala Leu Gly Tyr Ala Gly Pro Val Arg Arg Val Pro
1 5 10 15

Ser Leu Pro Gly Pro Pro Ala Thr Val Cys Pro Val Pro Ala Ser Glu
20 25 30

Phe Ser Gln His Arg Lys Arg Gly Leu Arg Thr Ile Gln Pro Val His
35 40 45

Ser Arg Glu Ser Leu Ser Val Ser Gln Arg Leu Met Gly Cys Leu Trp
50 55 60

Cys Arg Val Thr Pro Ala Ser Pro Cys Gly Gly Cys Ala Gly Gly Ala
65 70 75 80

Arg Pro Pro Pro Cys Ala Leu Ser Leu Ala Gln Gly Gln His Thr Ala
85 90 95

His Pro Leu Phe Phe Leu Pro Phe Pro Leu Ala Gln Pro Leu Val Val
100 105 110

Gly Val Thr Arg Gly Ala Glu Arg Ser Trp Arg Ser Arg Ala Cys Pro
115 120 125

Gly Pro Val Arg Glu Gly Gly Arg Gly Gln Gln His Pro Trp Arg Arg
130 135 140

Glu Asp Tyr Ile Ile Phe Ile Tyr His Met Pro Lys Ile Ala Leu Leu
145 150 155 160

Arg Ala Phe Asp Ile His Pro Lys Ile Phe Lys His Tyr Gly Ser Met
165 170 175

Ser Gly Cys Ile Ser Asn Met Lys Val Glu Ala Ser Cys Pro Ala Pro
180 185 190

Ser Pro Leu Trp Glu Asn Phe Val His Val Leu Ser Gln Leu Phe Gly
195 200 205

Lys Gly Gly Pro Ser His Cys Pro Leu Gly Gly Phe Asp Val His Cys
210 215 220

Val Gly Arg Ser Leu Pro Ser Ile Leu Phe Tyr Phe Cys Arg Ile Ser
225 230 235 240

Ala Gln Ser Gly Ser Ala Trp Gln Phe Ser Cys Ser Ala Arg Glu Val
245 250 255

Leu Cys Pro Gly Leu Cys Asp Phe Arg Arg Arg Glu Gly Ser Cys Arg
260 265 270

Pro Tyr Leu Gln Trp Leu Pro Pro Gly Ile Pro Val Cys Ser Leu Cys
275 280 285

Thr Val Gln Arg Arg Ser Gly Ser Trp Trp Arg Asp Gly Asp Pro Arg
290 295 300

Thr Met Ala Ser Thr Lys Ala Gly Gly Ala Cys Asp Arg Arg Trp Thr
305 310 315 320

Met Thr Gln Val Pro Ala Arg
325

<210> 212
<211> 310
<212> PRT
<213> Homo sapiens

<400> 212

His Glu Leu Ser Leu Pro Cys Gly Gln Ser Pro Val Ile Lys Lys Glu
1 5 10 15

His Thr Pro Ser Leu Thr Glu Thr Ser Leu Asn Lys Lys Asn Ala His
20 25 30

Gln Arg Asn Ile Glu Phe Lys Tyr Leu Glu Gln Met Ser Glu Ile Ser
35 40 45

His Lys Asn Leu Asn Arg Asn Trp Pro Ser Lys Ser Trp Glu Phe Gly
50 55 60

Asp Ala Asn Phe Ile Leu Ser Ile Leu Glu Gln Ser Lys Ile Asn Thr
65 70 75 80

Thr His Phe Ser Leu Arg Lys Ser Ala Tyr Leu Phe Asp Val Pro Ser
85 90 95

Gly Leu Glu Ile Pro Asn Lys Thr Leu Thr Leu Phe Ile Leu His His
100 105 110

Asn Ile Thr Val Asn Lys Asn Asn Leu Asn Leu Cys Ser Asn Phe Pro
115 120 125

Leu Trp Thr Gln Arg Lys Thr Gln Glu Lys Met Val Glu Cys Val Leu
130 135 140

Asn Lys Val His Tyr Leu Tyr Gln Lys Tyr Ala Val Ile Ser Thr Ser
145 150 155 160

Thr Pro Lys Cys Leu Phe Asn Phe Ala Met Met Tyr Lys Ile Leu Val
165 170 175

Thr Cys Gln Ser Ile Asn Phe Ser Gln Leu Ile Leu Lys Ala Glu Asp
180 185 190

Ser His His Phe Val Cys Phe Ser Val Asn Met Ile Val Phe Val Arg
195 200 205

Lys His Ile Tyr Pro Glu Ser Tyr Gly Pro Met Phe Leu Thr Phe Cys
210 215 220

Pro Arg Ser Val Cys Val Ala Ser Cys Val Cys Met Asp Val Asp Asn
225 230 235 240

Lys Leu Asp Ser Tyr Gln Glu Ser Lys Ile Lys Leu Leu Ser Cys Lys
245 250 255

Lys Phe Val Lys Tyr Val Asp Leu Ser Cys Leu Lys Leu Arg His Pro
260 265 270

Gly His Ser Leu Trp Arg Glu Asn Ser Pro Pro Leu His Val Asn Leu
275 280 285

Trp Val Gly Thr Gly Val Gln Gly Phe Arg Val Gly Leu Leu Leu Pro
290 295 300

Gly Met Ile Gln Lys Ile
305 310

<210> 213
<211> 314
<212> PRT
<213> Homo sapiens

<400> 213

Lys Ala Asp Lys Ile Thr Phe Leu Glu Ser Ser Ile Tyr Ser Leu Ile
1 5 10 15

Val Phe Leu Tyr Ile Thr Leu Ser Gln Leu Trp Ser Lys Glu His Ser
20 25 30

Thr Glu Glu Gly Gly Ser Leu Ile Phe Pro His Leu Val Thr Pro Met
35 40 45

Leu Glu Leu His Glu Ile Asp Asn Tyr Tyr Tyr Ile Val Ile Ser Phe
50 55 60

His Val Leu Ser Phe Ser Ser Ser Leu Leu Leu Phe Phe Lys Ser Arg
65 70 75 80

Lys Gln Asn Gly His Gln Leu His Glu His Cys Ser Lys Lys Ile Thr
85 90 95

Val Arg Pro Asn Leu Asn Cys Trp Leu Pro Gly Arg Ala Ile Leu Ile
100 105 110

Ala Tyr Lys Asp Gln Ile Lys Tyr Gln Ser Gln Val Val Arg Cys Pro
115 120 125

Cys Thr Glu His Asn Ile Val Tyr Lys Asp Val Glu Leu Leu Leu Leu
130 135 140

Leu Trp Phe Tyr Thr Val Ala His Asp Lys Glu Leu Ile Phe Tyr Leu
145 150 155 160

Asn Glu Val Leu Phe Tyr Ile Thr Tyr Phe Met Phe Phe Pro Gln Glu
165 170 175

Ser Phe Asn Leu Leu Arg Leu Arg Asp Ser Phe Lys Cys Phe Asp Pro
180 185 190

His Thr Leu Phe Ala Gly Cys Arg Arg Met Cys Met Ile Leu Thr Phe
195 200 205

Thr Ala Asn Leu Phe Phe Trp Met Gly Tyr Cys Asn Phe Leu Leu Glu
210 215 220

Asp His Thr Ser Ser Ser Met Phe Arg Arg Gly Leu His Leu Trp Phe
225 230 235 240

His Gly Trp Thr Leu Asp Pro Leu Trp Leu Ser Lys Ile Leu His Gln
245 250 255

Cys Asn Ser Phe Val Asn Gly Tyr Met Ile Gln Ala Gly Pro Ile Arg
260 265 270

Ala Leu Pro Arg Val Leu Leu Glu Leu Leu Gly Arg Glu Ile Leu Ser
275 280 285

Ser Thr Lys Val Ile Phe Trp Arg Asn His Asp Gln Glu Ser Gln Cys

290 295 300

Met Glu Asn Lys Ser Arg Glu Lys Lys Lys
305 310

<210> 214
<211> 320
<212> PRT
<213> Homo sapiens

<400> 214

Met His His Val Phe Ile Leu Trp Pro Leu Ile Asp Ser Trp Asp Val
1 5 10 15

Lys Glu Leu Ile Leu Tyr Thr Tyr Ala Asn Leu Lys Pro Ser Ile Ile
20 25 30

Ser Leu Thr Ser Pro Val Ser Ser Leu Cys Leu Cys Tyr Gln Gln Val
35 40 45

Asn Phe Ser Val Leu Pro His His Lys Pro Gln Leu Pro Leu His Met
50 55 60

Phe Pro Lys Leu Val Ala Asn Ser Val Phe Pro Gly Glu Cys Ile Lys
65 70 75 80

Tyr Pro Gly Ile His Cys Tyr Thr Val Ser Asn Gly Ser Ser Phe Ser
85 90 95

Leu Leu Trp Arg Arg Thr Pro Glu Glu Ser Thr Ser Pro Gly Pro Ala
100 105 110

Ala Ser Cys Met Gly Asn Leu Leu Leu Leu Leu Leu Gly Phe Thr Leu
115 120 125

His Ile Leu Ser Leu Arg Lys His Thr Lys Ser Phe His Val Phe Val
130 135 140

Pro Val Pro Met Pro Leu Leu Pro Gly Ile Pro Phe Phe Tyr Ser Tyr
145 150 155 160

Ser Leu Asn Lys Leu Phe Tyr Ser Phe Ser Ser Gly Pro Leu Pro Leu
165 170 175

Ile Gln Leu Arg Asn Asn Tyr Cys Leu Ser Pro Ser Lys Leu Ile Phe
180 185 190

Cys Leu Leu Phe Ser His His Thr Leu Pro Phe Thr Ser Val Ala Tyr
195 200 205

His Phe Phe Cys Tyr Leu Thr Asn Ala Ser Val Phe Ile His Ser Pro
210 215 220

Pro Arg Leu Tyr Ser Ser Trp Val Gln Ser Ile Ser His Ser Phe Leu
225 230 235 240

Cys Tyr Leu Cys Leu Ser Gln Cys Trp Leu Gln Ser Arg Tyr Phe Arg
245 250 255

Asp Ala Ile Ile Arg Val Arg Val Val Arg Ile Gly Glu Asn Glu Asp
260 265 270

Ser Met Val Leu Arg Cys His Ala Ser Cys Lys Glu Asn Met Lys Gly
275 280 285

His Phe Phe Phe Leu Gln Leu His Gly Leu Leu Gln Ser Leu Cys Leu
290 295 300

Leu Gly Leu Glu Leu Pro Ala Ile Ser Val Phe Val Arg Leu Leu Ile
305 310 315 320

<210> 215
<211> 317
<212> PRT
<213> Homo sapiens

<400> 215

Pro Val Asn Ala Lys Asp Ile Leu Phe Gly Leu Glu Ile Lys Leu Leu
1 5 10 15

Met Pro Ile Trp Pro Tyr Ala Leu Arg Thr Leu Leu His Asn Lys Ile
20 25 30

Ala Val Arg Val Thr Lys Trp Lys Met Asn Asn Met Tyr Arg Glu Arg
35 40 45

Ile Gln Lys Arg Asn Leu Tyr Phe Ile Phe Ser Lys Leu Pro Gln Ile
50 55 60

Cys Leu Arg Lys Leu Tyr Asp Leu Val Asn Arg Ile Leu Lys Thr Leu
65 70 75 80

Ile Tyr Lys Ser Gln Val Trp Ala Leu Val Thr Ser Leu Asn Asp Trp
85 90 95

Leu Ala Asp Asn Leu Ser Gly Ser Ser Tyr Leu Glu Ile Glu Asn Thr
100 105 110

Ser Leu Pro Phe Tyr Asn Ser Pro Gln Leu Phe Gln His Thr Gln Cys
115 120 125

Asp Lys Lys Pro Ser Gln Ala His Phe Ser Asn Asn Glu Phe Val Gly
130 135 140

Ser Phe Lys Cys Gln Gly Gln Gln Val Arg Ala Gly Ser Glu Ala Asp
145 150 155 160

Ile Phe Gly Glu His Gly Leu Ala Phe Ser Phe Leu Gly Thr Phe Val
165 170 175

Leu Trp Met Glu Ser Ile Leu Gly Gln Ala Glu Val Leu Leu Ser Trp
180 185 190

Trp Gln Asp Gly Tyr Ala Arg Gln Pro Ser Cys Leu Gln Arg Ala Cys
195 200 205

Leu Val Arg Ser Phe Gly Ile Ser Ser Asp Leu Met Asn Leu Gly Leu
210 215 220

Met Phe Ile Pro Gly Tyr Ile Ser Phe Ala Gln Val Asn Gly Tyr Val
225 230 235 240

Asp Cys His Thr Trp Val Ser Val Thr Thr Pro Gly Phe Ser Asp Gly
245 250 255

Val Ser Pro Lys Gly Pro Thr Arg Val Glu Glu Ser Gly Ser Trp Lys
260 265 270

Glu Ser Gln Gly Lys Gly Lys Gly Thr Asn Ala Arg Trp Ala Val Asn
275 280 285

Gly Ser Cys Pro Asn Phe Met Pro Glu Pro Leu Lys Gly Ile Phe Thr
290 295 300

Leu Thr Val Gly Ile Asn Ile Gly Arg Gly Asp Ala Trp
305 310 315

<210> 216
<211> 319
<212> PRT
<213> Homo sapiens

<400> 216

Arg Lys Lys Asp Asp Ser Ile His Val Arg Arg Asn Ser Ala Arg Met
1 5 10 15

Gln Lys His Lys Tyr Glu Lys Arg Val Tyr Cys Phe His Asn Lys Thr
20 25 30

Lys Thr Arg Lys Glu Ile Ala Cys Gly Lys Glu Lys Gln Ser Lys Lys
35 40 45

Arg Lys Thr Asn Leu His Val Ala Asn Leu Phe Val Thr Phe Gln Ile
50 55 60

His Met Ser Cys Ala Met Ile Thr Arg Gly Phe Pro Asp Lys Phe Cys
65 70 75 80

Phe Ser Ile Ile Phe Leu Gln Leu Tyr Lys His Gly Phe Tyr Ser Asp
85 90 95

Asn Leu Ser Phe Asp Ile Phe Phe Ile Asp Tyr Gln Arg Ile Leu Glu
100 105 110

Thr Asn Gln Ala Gln Tyr Phe Asn Phe Gln Phe Ser Leu Pro Val Ile
115 120 125

Leu Leu Pro His Thr Ala Ser Thr Pro Ser Trp Tyr Gln Leu Lys Lys
130 135 140

Tyr Tyr Val Arg Met Thr Ser Val Thr Leu Val Leu Phe Ile Leu Asn
145 150 155 160

His Ser Glu Pro Tyr His Cys Val Leu Asn Leu His Leu Thr Asp Pro
165 170 175

Tyr Leu Cys Ser Ser Ser Ser Ala Leu Asp Leu Cys Phe Gln Ala Leu
180 185 190

Arg Phe Tyr Asn Val Ile Asn Pro Leu Ser Leu Ile Phe Ser Ser Pro
195 200 205

Leu Thr Cys Met Cys Val Glu Ser Val Tyr Met Leu Glu Asn Tyr Thr
210 215 220

Thr Phe Thr Arg Phe Ile Leu Leu Val Tyr Leu Thr Leu Thr His Phe
225 230 235 240

Tyr Ser Leu Gly His Tyr Leu Cys Met Ala Tyr Ala Glu Val Gly Ser
245 250 255

Gly His Tyr Lys His Gln Glu Thr Ile Ser Ile Thr Pro Cys Ile His

260 265 270

Val His Val Val Leu Lys Tyr Asn Val Lys Tyr Arg Glu Val Thr Leu
275 280 285

Gly Leu Asn Ser Gly Val Ser Ala Arg Leu Gly Leu Ile Thr Thr Leu
290 295 300

Leu Leu Ala Asn Tyr Ala Ser Leu Asn Pro Cys Ala Ser Lys Leu
305 310 315

<210> 217
<211> 313
<212> PRT
<213> Homo sapiens

<400> 217

Trp Pro Gln Ile Ser Phe Pro Pro Tyr Val Pro Leu Val Ser Thr Asn
1 5 10 15

Leu Phe Leu Pro Tyr Trp Ser Gly Gln Cys Pro Pro Asp Thr Ala Val
20 25 30

Leu Pro Thr Gly Leu Leu Ser Ser Phe Leu Ser Val Ile Ile Leu Ala
35 40 45

Cys Leu Trp Leu Lys Ala His Leu Cys Gly Pro Gln Arg Asn Tyr Leu
50 55 60

Pro Leu His Ser Ser Ser Trp His Leu Ser Leu Met Asp Ser Tyr Tyr
65 70 75 80

Pro Leu Leu Leu Leu Cys Ala Phe Met His Ile Ile Leu Ala Pro Pro
85 90 95

Asp Gln Leu Ser Leu Gly Gln Gly Phe Asp Leu Val Pro Ile Tyr Ser
100 105 110

Ser Pro Arg Ala Ser Leu Leu His Thr Val Gly Trp Gly Lys Ile Phe
115 120 125

Ala Tyr Ala Asp Asp Leu Arg Lys Ile Ile Leu Gln Thr Gly Glu Val
130 135 140

Lys Ile Ser Leu Ser Cys Ser Ile Trp Asn Glu Leu Val Ala Gly Asn
145 150 155 160

Gln Leu Glu Val Ser Ser Glu Gly Asn Thr Trp Thr Tyr Pro Leu Leu
165 170 175

Gln Val Ser Tyr Leu Tyr Lys Asp Cys Val Pro Val Thr Asn Leu Phe
180 185 190

Leu Asn His Trp Cys Cys Tyr Leu Gln Glu Gly Leu Gly Gln Ile Cys
195 200 205

Glu Glu Thr Ser Met Tyr Thr His Pro Tyr His Leu Lys Asn Lys Phe
210 215 220

Val Cys Val Pro Leu Met Lys Tyr Glu Glu Arg Ser His Ser Phe Gln
225 230 235 240

Ser Thr Gln Ala Leu Cys Leu Gly Leu Leu Ala Thr His Ala Lys Ile
245 250 255

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Leu Tyr Gln His Phe Val Lys Pro Thr Ile Leu Thr Val Pro Ala Leu
            260                 265                 270

Gln Pro Val Ile Asp Ser Asn Phe Asn Ser Pro Leu Val Ala Ile Ser
        275                 280                 285

Asp Ala Gln Cys Leu Cys Leu Leu Pro Leu Cys Ile Pro Ser Pro Ala
    290                 295                 300

Leu Asn Ser Ala Gly Cys Ile Gln Glu
305                 310

<210>  218
<211>  313
<212>  PRT
<213>  Homo sapiens

<400>  218

Thr Cys Ser Ser Thr Asp Ser Lys Val Ile Leu Lys Ser Gln Leu Asn
1               5                   10                  15

Val Ile Thr Arg Cys Arg Asp Ser Arg Tyr Val Tyr Ser Glu Arg Asn
            20                  25                  30

Cys Ser Pro Ser Val Ile Leu Ile Lys Val Lys Ser Phe Gln Asn Ala
        35                  40                  45

Met Val Gly Gln Thr Asn Arg His Ser His Ser Lys Arg Glu Lys Glu
    50                  55                  60

Gly Ile Leu Gln Gln Gln Gln Ser Lys Arg Ile Leu Arg Leu Gln Asn
65                  70                  75                  80

Asn Leu Leu Leu Met Pro His Leu Pro Ile Phe Gln Ala His Leu Gly
                85                  90                  95

Arg Arg Trp Ala Pro Lys Ala Leu Gly Val Pro Val Pro Ala His Met
            100                 105                 110

Thr Ala Leu Thr Tyr Ser His Met Pro Gly Trp Lys Cys Pro Leu Val
        115                 120                 125

Ala Leu Leu Val Tyr Gly Gln Arg Val Gly Leu Leu Leu Leu Cys Gln
    130                 135                 140

Ala Gln Pro Trp Arg Leu Phe Val Val Ala Pro Pro Leu Cys Gln Phe
145                 150                 155                 160

Phe Ala Ala Ser Arg Leu Ser Arg Ala Ser Phe Glu Ile Cys Val Glu
                165                 170                 175

Ser Ala Phe Pro Leu Trp Tyr Cys Thr Val Cys Pro Gly Gly Asp Asp
            180                 185                 190

Thr Arg Thr Leu Pro Thr Phe Ile Ile Cys Ala Leu Gln Lys Gly Gly
        195                 200                 205

His Trp Ser Pro His His Thr Trp Thr Leu Trp Ser His Ala Trp Asn
    210                 215                 220

Asp Ala Val Leu Cys Gln Lys Ala Gly Ser Arg Asp Glu Val Ala Gly
225                 230                 235                 240
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Arg Lys Cys Ala Pro Val Gly Ile Leu Gly Pro Ser Phe Asp Leu Val
245 250 255

Leu Ser Pro Arg Pro Trp His Ala Gly Pro Val Met Gly Ala Ala Ala
260 265 270

Val Met Met Ser Glu Met Leu Leu Val Gly Val Ile Pro Pro Leu Pro
275 280 285

Lys Ala Pro Gly Phe Cys Ser Ser Met Leu Ile Ser Asn Gly Cys Trp
290 295 300

Ala Thr Ser Leu Val Phe Ser Pro Lys
305 310

<210> 219
<211> 318
<212> PRT
<213> Homo sapiens

<400> 219

His Arg Asn Ile Leu Gln Asn Phe Asn Ile Thr Val Leu Asn Ser Val
1 5 10 15

Lys Thr Lys Asp Asn Pro Leu His Pro Asn Met Thr Ala Phe Asn Ile
20 25 30

Leu Leu Tyr Phe Ser Leu Phe Ala Met Tyr Ile Ile Leu Gln Ser Cys
35 40 45

Asn His Thr Gln Tyr Met Ile Leu Ser Cys Phe Pro Thr Tyr His Tyr
50 55 60

Arg Tyr Phe Tyr Cys Tyr Ile Val Phe Met Val Val Ile Val Asn Ser
65 70 75 80

Tyr Ala Val Ile Val His Ile Glu Val Leu Tyr Leu Leu Ser Tyr Pro
85 90 95

Ile Ile Phe Lys Gln Phe Leu Ile Ser Phe Tyr Asn Lys His Gly His
100 105 110

Ile Ser Asp Arg Gly Val Leu Phe His Ile Leu Thr Tyr Phe Ser His
115 120 125

Ser Val Thr Ile Thr Pro Lys Asn Thr Asn Phe Leu Ser Leu Asp Val
130 135 140

Tyr Phe Gln Lys Ile Phe Lys Arg Cys Ile Asn Leu Leu Cys Ser Trp
145 150 155 160

Cys Lys Arg Pro Phe Cys His Cys Phe Leu Glu Ser Arg Ala Ser Lys
165 170 175

Ser Arg Asp Met Trp Leu Gly Gly Arg Asn Pro Ala Trp Gly Arg His
180 185 190

Ser Val Lys Asn Ser Ser Ser His Trp Tyr Thr Gly Phe Ile Phe Leu
195 200 205

Cys Phe Leu Gln Thr Glu Gln Leu Ile Thr Leu Trp Val Leu Phe Val
210 215 220

Phe Thr Ile Val Gly Asn Ser Val Val Leu Phe Ser Thr Trp Arg Arg

```
225                 230                 235                 240

Lys Lys Lys Ser Arg Met Thr Phe Phe Val Thr Gln Leu Ala Ile Thr
                245                 250                 255

Gly Lys Leu Cys Lys Glu Ala Gly Ser Tyr Met Ser Pro Tyr Gly Phe
            260                 265                 270

Leu Leu Leu Met Asn Phe Ile Lys Lys Lys Lys Met Arg Ile Gly Gln
        275                 280                 285

Phe Gly Asn Asn Phe Lys Asn Ile Lys Pro Ile Phe Glu Tyr Phe Leu
    290                 295                 300

Trp His Thr His Ile Met Pro Leu Arg Phe His Tyr Lys Ser
305                 310                 315

<210>  220
<211>  320
<212>  PRT
<213>  Homo sapiens

<400>  220

Ile Ile Pro Ser Val Ile Phe Phe Tyr Cys Arg His Cys Lys Ser Leu
1               5                   10                  15

Asn Leu Asp Lys Ser Tyr Ser Gly Gln Asn Lys Asn Phe Thr Val Ile
            20                  25                  30

Asn Val Cys Ser Cys Thr Cys Glu Val Lys Ser Phe Ser Leu Leu Ser
        35                  40                  45

Asn Ser Tyr Val Pro Asn Ile Phe Ser Lys Phe Leu Lys Thr Tyr Asn
    50                  55                  60

Gly Glu Lys Asn Asn Pro Phe Ser Ser Pro Ala Ser Leu Met Lys Asn
65                  70                  75                  80

Ser His Phe Ser Leu Phe Leu Leu Phe Leu Leu Val Val Phe His Ile
                85                  90                  95

Ser Cys Leu Ser Ala Val Ser Cys Phe Met Gln Phe Arg Pro Tyr Leu
            100                 105                 110

Leu Thr Ser Leu Ser Phe Gln Tyr Lys Asp Ser Cys Ile Phe Ser Phe
        115                 120                 125

Asn Phe Thr Phe Leu Asn Ser Pro Phe Pro Phe Cys Asp Pro Gly Ile
    130                 135                 140

Ser Gly Val Leu Phe Phe Phe Ile Leu Pro Asp Phe Ile Tyr Ile Cys
145                 150                 155                 160

Val Tyr Ser Phe Leu Leu Phe Phe Lys Leu Lys Thr Cys Leu Ser Ser
                165                 170                 175

Lys Ser Gly Ser Phe Phe Phe Ser Trp Arg Pro Leu Ser Gln Asn Pro
            180                 185                 190

Leu Ser Phe Cys Phe Asn Glu Asp Tyr Met Leu Ser Leu Trp Leu Pro
        195                 200                 205

Ser Cys His Trp Ser Ser Ser Leu Cys Cys Tyr Pro Gly Leu Lys Leu
    210                 215                 220
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Leu Phe Leu Asp Pro Ile Leu Ser Leu Ser Trp Phe Ile Thr Leu Phe
225 230 235 240

Cys Trp Gly Thr Ser Ser Cys Met Trp Asn Val Met Ser Ala Ser Leu
245 250 255

Cys Phe Lys Met Tyr Ile Phe Cys Pro Leu Phe Asp Leu Ala Glu Asn
260 265 270

Arg Ile Leu Asp Cys Lys Ile Gln Lys Leu Leu Gln Arg Leu His His
275 280 285

Arg Gln Lys Asn Leu Cys Thr His Phe Pro Pro Thr Ser Ser Pro Pro
290 295 300

Ala Ala Arg Ser Asn His Glu Ser Phe Cys Gln Asn Arg Phe Ala Tyr
305 310 315 320

<210> 221
<211> 318
<212> PRT
<213> Homo sapiens

<400> 221

Cys Ile Lys Val Phe Ile Leu Lys Gly Lys Ala Thr Met Ile Ala Gln
1 5 10 15

Leu Trp Tyr Ile Ile Ile Ser His Ile Ile Phe Leu Leu Leu Glu Lys
20 25 30

Gly Ile Tyr Asp Phe Ser Arg Met His Thr Glu Lys Pro Leu Cys Ile
35 40 45

Ile Leu Cys Glu Ser Lys Leu Cys Thr Tyr Phe Glu Val Ile Cys Ile
50 55 60

Leu Cys Arg Arg Lys Glu Asn Asn Leu Leu Tyr Phe Val Cys Gly Ile
65 70 75 80

Gly Asn Val Phe Leu Thr Lys Pro Lys Asn Ile Ser His Ser Lys Gly
85 90 95

Lys Met Gly Leu Asn Glu Lys Met Val Asp Leu Lys Tyr Gly Gly Arg
100 105 110

Phe Phe Trp Gly Thr Leu Asp Leu Ile Met Phe Phe Ser Ile Pro Phe
115 120 125

Leu Gln Met Phe Ile Ile Leu Leu Leu Phe Ile Tyr Ala Ala Ile Ile
130 135 140

Tyr Val Cys Ser Cys Phe Ser Cys Ser Gln Thr Leu Tyr Asn Val Ile
145 150 155 160

Ile Gln His Glu Ser Phe Ser Ile Leu Leu Phe Leu Val Asn Ile Ile
165 170 175

Ile Trp Gly Tyr Trp Cys Thr His Cys Gln Phe Ile His Phe Asn Tyr
180 185 190

Ser Thr Gly Phe Trp Ser Met Asn Ile Ser Tyr Phe Ile Tyr Leu Tyr
195 200 205

Pro Ile Asp Val Tyr Leu Val Pro Ile Phe Ala Val Lys Asn Asn Ala
210 215 220

Ala Ile Lys Pro Ser Gly Ile Cys Phe Ser Lys Cys Ile Pro Arg Ser
225 230 235 240

His Arg Phe Ser Gly Cys His Ser Leu Lys Leu Leu Gly Lys Thr Val
245 250 255

Arg Ile Leu Gly Asn Leu Leu Asn Leu Thr Trp Leu Asn Phe Leu Ala
260 265 270

Gln Met Arg Val Val Leu Asp Leu Ile Lys Asn Met Val Ile Phe Cys
275 280 285

Glu Thr Leu Ala Asn Tyr Asp Asn Lys Trp Ser Leu Gly Ile Ser Val
290 295 300

Ile Thr Ala Ile Lys Arg Gly Leu Lys Tyr Pro Lys Glu Lys
305 310 315

<210> 222
<211> 317
<212> PRT
<213> Homo sapiens

<400> 222

Asn Tyr Leu Ser Asp Cys His Ser Phe Met Glu Leu Ser Val Asn Lys
1 5 10 15

Val Leu Leu Tyr Val Asn Met Arg Leu Ile Phe Phe Leu Ser Leu Leu
20 25 30

Phe Gly Leu Tyr Phe Phe Gln Val Arg Ala Ile His Gly Ser Ala Ser
35 40 45

Thr Asp Gln His Leu Leu Ser Tyr Phe Ala Ile Trp Leu Pro Gly Leu
50 55 60

Arg Glu Cys Phe Phe Asn Leu Tyr Trp Trp His Cys Trp Leu Leu Ile
65 70 75 80

Leu Leu Phe Val Leu Ala Arg Leu Leu Phe Lys Arg Arg Val Ile Asn
85 90 95

Ser Val Leu Arg Ala Glu Val Lys Tyr Arg Met Glu Leu Glu Glu Asn
100 105 110

Glu Ala Ser Ile Ser Val Lys Lys Ser Phe Ile Lys Ala Val Gly Asp
115 120 125

Arg Glu Leu Gly Val Thr Ile Leu Val Pro Ile Val Met Val His Pro
130 135 140

Gly Lys Ile Gln Gly Lys Arg Glu Ser Leu Trp Lys Ser Phe Gly Cys
145 150 155 160

Val Leu Ser Cys Phe Arg Lys Leu Ala Asn Phe Tyr Thr Ser Val Phe
165 170 175

Arg Leu Ser Cys Leu Asp Thr His Pro Thr Gln Ser Ala Gln Gln Tyr
180 185 190

Phe Leu Cys Ser Ser Leu Ser Pro Gly Ile Arg Met Ala Pro Leu Gly

```
        195                     200                     205

Glu Leu Leu Ser His Met Ile Lys Asp Leu His Tyr Phe Leu Ser Lys
    210                     215                     220

Ser Arg Arg Lys Val Gly Glu Leu Ala Trp His Leu Ala Gly Thr Tyr
225                     230                     235                     240

Asn Thr Ala Ser Thr Trp His Leu Leu Asp Arg Leu Pro Leu Pro Thr
                245                     250                     255

Val Val Thr Thr Ser Met Gly Gly Gly Trp Cys Cys Thr Val Pro Met
            260                     265                     270

Gly Trp Cys Ala Cys Ser Pro Met Pro Pro Ala Leu Pro Gln Cys Cys
        275                     280                     285

Leu Leu Gln Ser His Leu Phe Arg Trp Ser Ile Leu Ile Glu Lys Val
    290                     295                     300

Leu Gly Thr Ile Cys Leu Lys Cys Ser Pro Ala Asn Val
305                     310                     315

<210>  223
<211>  314
<212>  PRT
<213>  Homo sapiens

<400>  223

Leu Cys Tyr Cys Val Ile Ile Ile Ile Val Pro Phe Pro Ser Ile Pro
1               5                   10                  15

Gln Thr His Thr Tyr Val Glu Ile Leu Arg Gly Asp Asp Val Leu Phe
            20                  25                  30

Thr Ser Ala Cys Leu Met Leu Ser Pro Val Leu Gly Thr Asn Ala Ile
        35                  40                  45

Val Phe Leu Glu His Glu Ile His Gln Lys His Glu Trp Ile Trp Trp
    50                  55                  60

Gly His Lys Arg Leu Thr Pro Gly Ser Arg Asn Leu Gly Gly Glu Thr
65                  70                  75                  80

Ser Gly Leu Glu Gly Ala Glu Asp His Cys Val Arg Ser Thr Trp Phe
                85                  90                  95

Trp Leu Ala Gly Leu Ala Arg Met Gln Arg Ser Phe Trp Val Leu Leu
            100                 105                 110

Lys Phe Lys Thr Thr Ile Ile Ile Asn Ile His Leu Val Leu Thr Met
        115                 120                 125

Cys Gln Ser Leu Ile Ala Phe Tyr Val Phe Ser His Ser Ser Lys Phe
    130                 135                 140

Gly Leu Asp Ile Phe Pro Val Tyr Thr Ile His Met Arg Lys Arg Val
145                 150                 155                 160

Glu Gln Gly Gly Ala Glu Thr Cys Pro Arg Ile His Ser Lys Asn Gly
                165                 170                 175

Asn Trp Asp Trp Ser Pro Arg Asp Ser Cys Phe Leu Asp Phe Val Phe
            180                 185                 190
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Leu Ile Ser Leu Pro Leu Arg Leu Phe Ile Asp Ile Phe Thr Phe Tyr
195 200 205

Phe Glu Ile Ile Val Asp Ser Gln Glu Val Thr Arg Glu Arg Ser Cys
210 215 220

Val Leu Phe Thr Gln Ile Ser Pro Met Leu Arg Phe Tyr Ile Thr Val
225 230 235 240

Ile Gln Tyr Glu Asn Gln Glu Thr Asp Ile Gly Ser Ile Tyr Val Tyr
245 250 255

Thr Ser Met Pro Phe His His Val Met Pro Pro Ser Pro Ser Cys Arg
260 265 270

Thr Val Pro Ser Pro Arg Arg Ser Ala Thr Cys Cys Ser Phe Lys Val
275 280 285

Ile Pro Ala Leu Phe Pro Val Pro Thr His Cys His Tyr Ala Pro Leu
290 295 300

Val Thr Thr Asn Leu Phe Ser His Leu Tyr
305 310

<210> 224
<211> 321
<212> PRT
<213> Homo sapiens

<400> 224

Lys Pro Ser Ser Gly Cys Gly Gly Trp Met Trp Asp Trp Met Gly Thr
1 5 10 15

Gln Lys Asn Ile Lys Thr Met Ala Thr Val Ile Ile Ile Val Ile Asn
20 25 30

Ser Gln Asp Asn Asn His Leu Ala Thr Val Ala Met Tyr Leu Lys Asp
35 40 45

Tyr Ser Leu Gly Val Phe Phe Leu Met Ser Met Glu Gln Asp Asp Trp
50 55 60

Ala Phe Glu Asp Ile Lys Glu Thr Lys Gly Pro Asp Cys Asn Gln Arg
65 70 75 80

Phe His Ser His Arg Pro Gly Phe Thr Trp Gln His Thr Phe Trp Thr
85 90 95

Phe Phe Phe Phe Ser Gly Lys Glu Thr Gly Ser Val Glu Asn Gly Arg
100 105 110

Met Arg Thr Asn Cys Arg Ala Leu Pro His Ser Trp Thr Leu Ser His
115 120 125

Ser Ser Arg Trp Gly Pro Pro Ala His Cys Trp Leu Cys Pro Pro Gln
130 135 140

Phe Leu Arg Ile His Thr Asp Phe Ala Lys Ile Leu Arg Tyr Val Gly
145 150 155 160

His Glu Leu Trp Val Cys Ala His Leu Val Pro Ser Leu Tyr Ser Thr
165 170 175

Leu His Ser Ser Gly Val Phe Leu Thr Ala Gly Ala Thr Phe His Leu
180 185 190

His His Tyr Tyr Ile Lys Trp Ala Ser Ile Phe Pro Ser Glu Phe Gln
195 200 205

Pro Leu Ser Gly Asn Leu Thr Phe Phe Leu Val Ser Phe Ala Leu Arg
210 215 220

Phe Cys Pro Phe Tyr Cys Ser Asn Glu Phe Thr Gln Pro Ser Ile Pro
225 230 235 240

His Glu Ser Gly Gln Asp Pro Val Thr Cys Asp Ser His Thr Asp Cys
245 250 255

Val Arg Val Thr Pro Pro Val Pro Gly Phe Pro Glu Pro Cys Leu Ser
260 265 270

Arg Leu Thr Gly Gln Ser Trp Asp Met Asn Trp Ala Pro Glu Leu Ala
275 280 285

Leu Phe Val Ser Arg Ser Ser Arg Cys Leu Cys Arg Leu Pro Asn Pro
290 295 300

Cys Ser Trp Ala Trp Val Ala Glu Ser Ala Gly Arg Leu Trp Cys Met
305 310 315 320

His

<210> 225
<211> 314
<212> PRT
<213> Homo sapiens

<400> 225

Leu Cys Tyr Cys Val Ile Ile Ile Ile Val Pro Phe Pro Ser Ile Pro
1 5 10 15

Gln Thr His Thr Tyr Val Glu Ile Leu Arg Gly Asp Asp Val Leu Phe
20 25 30

Thr Ser Ala Cys Leu Met Leu Ser Pro Val Leu Gly Thr Asn Ala Ile
35 40 45

Val Phe Leu Glu His Glu Ile His Gln Lys His Glu Trp Ile Trp Trp
50 55 60

Gly His Lys Arg Leu Thr Pro Gly Ser Arg Asn Leu Gly Gly Glu Thr
65 70 75 80

Ser Gly Leu Glu Gly Ala Glu Asp His Cys Val Arg Ser Thr Trp Phe
85 90 95

Trp Leu Ala Gly Leu Ala Arg Met Gln Arg Ser Phe Trp Val Leu Leu
100 105 110

Lys Phe Lys Thr Thr Ile Ile Ile Asn Ile His Leu Val Leu Thr Met
115 120 125

Cys Gln Ser Leu Ile Ala Phe Tyr Val Phe Ser His Ser Ser Lys Phe
130 135 140

Gly Leu Asp Ile Phe Pro Val Tyr Thr Ile His Met Arg Lys Arg Val

145 150 155 160

Glu Gln Gly Gly Ala Glu Thr Cys Pro Arg Ile His Ser Lys Asn Gly
165 170 175

Asn Trp Asp Trp Ser Pro Arg Asp Ser Cys Phe Leu Asp Phe Val Phe
180 185 190

Leu Ile Ser Leu Pro Leu Arg Leu Phe Ile Asp Ile Phe Thr Phe Tyr
195 200 205

Phe Glu Ile Ile Val Asp Ser Gln Glu Val Thr Arg Glu Arg Ser Cys
210 215 220

Val Leu Phe Thr Gln Ile Ser Pro Met Leu Arg Phe Tyr Ile Thr Val
225 230 235 240

Ile Gln Tyr Glu Asn Gln Glu Thr Asp Ile Gly Ser Ile Tyr Val Tyr
245 250 255

Thr Ser Met Pro Phe His His Val Met Pro Pro Ser Pro Ser Cys Arg
260 265 270

Thr Val Pro Ser Pro Arg Arg Ser Ala Thr Cys Cys Ser Phe Lys Val
275 280 285

Ile Pro Ala Leu Phe Pro Val Pro Thr His Cys His Tyr Ala Pro Leu
290 295 300

Val Thr Thr Asn Leu Phe Ser His Leu Tyr
305 310

<210> 226
<211> 312
<212> PRT
<213> Homo sapiens

<400> 226

Gly Ala Arg Gly Gly Glu Ala Ser Thr Ser Leu Glu Ser Gln Val Glu
1 5 10 15

Asp Thr Ala Glu Gln Thr Ser Asn Leu Ile Thr Val Thr Leu Ile His
20 25 30

Pro Gln Leu Ala Lys Tyr Thr Leu Ile Val Asn Phe Leu Pro Leu Trp
35 40 45

Ser Leu Ser Asp Ile Ser Thr Asp Leu Leu Phe Ile Leu Leu Arg Leu
50 55 60

Arg Asn Ile Ile Arg Ile Leu Gln His Leu Gly Glu Ile Ile Glu Ser
65 70 75 80

Ala Met Val Ser Phe Ala Asp Ile Tyr Ser Trp Ser Lys Trp Asn Thr
85 90 95

Asn Gln Asn Trp Leu Pro Tyr Ile Leu Gln Arg Pro Thr Gly Gly Lys
100 105 110

Gly Leu Trp Lys Val Cys Phe Ala Thr Arg Gln Ile Leu Asp His Pro
115 120 125

Val Ser Gly Ser Ile His Ser Phe Pro Asp Ser Pro Asp Asp Ile Pro
130 135 140

```
Pro Ser Phe Thr Tyr Ile Asn Ser Thr Val Pro Ile Cys Tyr Ile Ala
145                 150                 155                 160

Ser Phe Leu Leu Phe Ile Ile Cys Leu Pro His Gln Asn Ala Ser Ser
                165                 170                 175

Ile Trp Ala Val Ala Thr Leu Phe Thr Val Tyr Leu Ser Val Ser Met
            180                 185                 190

Lys Ser Asp Ile Met Pro Gly Ile Tyr Tyr Glu Leu Asn Asn Tyr Val
        195                 200                 205

Asn Glu Ile Met Arg Lys Ser Cys Leu Ile Thr Cys Gln Pro Tyr Asn
    210                 215                 220

Ala Ser Gln Phe Phe Pro Leu Gln Phe Leu His Leu Asn Trp Ile Thr
225                 230                 235                 240

Gln Met Leu Thr Leu Trp His Cys Trp Asn Asn Tyr Leu Lys Ser Cys
                245                 250                 255

Lys Phe Ile Ala Tyr Trp Lys Cys Gly Ser Glu Cys Asp Thr Pro Gln
            260                 265                 270

Tyr Gly Val Leu Val Val Leu Thr Glu Gly Asn Lys Ser Phe Arg Asn
        275                 280                 285

Lys Val Phe Leu Ala Phe Ser His Leu Ser Phe Ser Cys Ser Pro Phe
    290                 295                 300

Phe Pro Lys Ala Asp Gln Arg Asn
305                 310
```

<210> 227
<211> 321
<212> PRT
<213> Homo sapiens

<400> 227

```
Gly Cys Ser Pro Glu Asp Asp Leu Gly Cys Ser Gly Val Asn Tyr Pro
1               5                   10                  15

His Phe Leu Arg Ala Ser Met Trp His Ser Trp Pro Trp Ala Ser Ala
            20                  25                  30

Cys Pro Ala Asn Ala Gln Pro Val Pro Ala Val Pro Pro Pro Leu Ala
        35                  40                  45

Ala Gln Pro Gln Val Trp Pro Ser Gly Leu Tyr Pro Arg Pro Pro His
    50                  55                  60

Leu Pro Thr Leu Phe Leu Cys Ser Glu Leu Ser Thr Ala Ala Pro Ala
65                  70                  75                  80

Pro Trp Leu Pro Leu Ile Leu Cys Leu Val Ser Phe Phe Gly His Ser
                85                  90                  95

Phe Ala Ala Thr Leu Tyr Trp Ile Thr Leu Leu Gly Val Leu Ile Ile
            100                 105                 110

Ser His Pro Leu Leu Leu Pro Asn Gly Pro Ser Thr Ile Ser Phe His
        115                 120                 125
```

Arg Leu Asn Gly Lys Gly Gly Val His Ile His Arg Ile Lys Gln Val
130 135 140

Met Pro Leu His Ser Gly Val Cys Asp Asp Asn Phe Tyr Ala Phe Tyr
145 150 155 160

Thr Asn Ile Phe Val Ser Leu Cys Phe Leu Pro Cys Leu Arg Ala Leu
165 170 175

Gln Gly Leu Ala Leu Gly His Pro Val Leu His Thr His Thr Arg Thr
180 185 190

His Thr Arg Thr Cys Thr His Val His Thr His Ala His Thr His Thr
195 200 205

His Thr His Lys His Thr His Ser Leu Ala Leu Ala Asn Ala Ser Leu
210 215 220

Ala Leu Thr Thr Asn Val Ser Ala Ser Asp Leu His Asn Leu Ile Trp
225 230 235 240

Leu Phe Leu Phe Leu Gly Val Ile Cys Leu Pro Glu Gly Arg Ala Asn
245 250 255

Ser Pro Ala Ile Pro Ala Ala Tyr Ser Leu Pro Val Pro Ser Phe Pro
260 265 270

Arg Arg Gln Gln Thr Glu Arg Gly Lys Arg Tyr Lys Glu Ala Trp Gly
275 280 285

Trp Gly Lys Glu Ser Ser Tyr Leu Thr Ser Ala Pro Leu Thr Leu Leu
290 295 300

Gly Glu Val Pro Thr His Ser Ser Gly Met Thr Thr Arg Met Val Ser
305 310 315 320

Leu

<210> 228
<211> 123
<212> PRT
<213> Homo sapiens

<400> 228

Asp Cys Ala Ala Ala Leu Pro Gly Gln Ser Lys Thr Pro Phe Gln Lys
1 5 10 15

Lys Lys Lys Lys Lys Lys Glu Arg Lys Glu Phe Met Asp Val Ile Val
20 25 30

Lys Gly Leu Val Pro Ser Pro Ile Ser Cys Phe Pro Ser Cys His Val
35 40 45

Thr Cys Trp Phe Pro Phe Thr Phe Cys His Asp Trp Lys Leu Pro Gly
50 55 60

Ala Ser Pro Glu Ala Lys Gln Met Pro Gly Pro Cys Phe Leu Tyr Ser
65 70 75 80

Leu Leu Asn Pro Glu Pro Asn Lys Pro Leu Phe Ile Thr Asn Tyr Leu
85 90 95

Gly Ser Asp Ser Pro Leu Gln Cys Lys Trp Thr Asn Thr Pro His Asp

100 105 110

Leu His Pro Gln Thr Thr Gly Gly Thr Gln His
115 120

<210> 229
<211> 210
<212> PRT
<213> Homo sapiens

<400> 229

Ser Ala Cys Gly Gly Phe Asn Gly Leu His Phe Tyr Ser Asn Ile Ser
1 5 10 15

His Gln Leu Tyr Ile Tyr Tyr Leu Lys Val Phe Leu Phe Ile Val Phe
20 25 30

Gln Phe Ile Phe Gln Ile Arg Ser Lys Gln Asn Tyr Ser Trp Arg Leu
35 40 45

Cys Cys Leu His Pro Gln Tyr Gln Met Phe Met Ala Ser Thr Glu Pro
50 55 60

Gly Val Ser Met Glu Ser Leu Arg Asp Cys Leu Ser Phe Ser Glu Glu
65 70 75 80

Ser Val Met Phe Ser Ile Pro Glu Glu Ala Glu Ile Thr Leu His Tyr
85 90 95

Phe Phe Glu Leu Cys Ala Gly Arg His Gly Ser Glu Ile Cys Leu Ser
100 105 110

Asp Ser Asn Ser Ser Ser Ile Cys Val Leu Val Phe Val Val Ala Phe
115 120 125

Cys Ile Gln Leu Pro Asp Asn Phe Phe Leu Met Phe Cys Cys Asn Leu
130 135 140

Val Lys Leu Leu Phe Tyr Lys Leu Met Phe Trp Tyr Phe Gly His Gln
145 150 155 160

Ile Leu Ala Arg Gly Lys Ile Arg Thr Arg Ser Thr Ser Cys Lys Thr
165 170 175

Lys Leu Ile Phe Leu Val Asp Phe Trp Asn Gly Leu Phe Cys Phe Pro
180 185 190

Ile Cys Val Tyr Phe Leu Lys Ser Cys Arg Cys Ile Tyr Glu Tyr Leu
195 200 205

Phe His
210

<210> 230
<211> 204
<212> PRT
<213> Homo sapiens

<400> 230

Val Ile Asn Ser Ser Cys Pro Ser Ile Ile Gly Leu Gly Thr Pro Gly
1 5 10 15

Phe Ser Cys Ser Ser Ser Val Ile Gly Arg Lys Ile Gly His Trp Leu

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            20                      25                      30

Lys Gln Ile Leu Ser Phe Leu Gly Val Val Phe Thr Leu Lys Ala Leu
        35                      40                      45

Arg Pro Leu Gly Gly Ser Ala Ile Leu Gln His Gly Arg Cys Pro His
    50                      55                      60

Thr Trp Met Ala Ala Phe Tyr Tyr Tyr Ser Leu Asp Thr Gly Phe Phe
65                      70                      75                      80

Ala His Val Tyr Thr Leu Gly Ser Ile Cys Tyr Pro Phe Phe Thr Leu
                85                      90                      95

Lys Gln Val Ile Gly Lys Phe Ile Ser Ile Trp Lys Thr Asn Asp Gln
            100                     105                     110

Lys Asn Pro Ser Asn Pro Lys Phe Thr Glu Ala Arg Leu Leu Lys Arg
        115                     120                     125

Lys Asp Ile Phe Leu Cys Arg Lys Val Met Phe His Arg Gly Phe Cys
    130                     135                     140

Asn Ala Leu Thr Leu Asp Arg Ser Pro Pro Ser Ile Leu Gly Ile Thr
145                     150                     155                     160

Ser Phe His Phe Ser Cys Lys His Ser Ser Pro Cys Thr Leu Gln Asp
                165                     170                     175

Phe Ser Leu Phe Glu Ile Gly Leu His Ser Val Gly Arg Gly Asp Trp
            180                     185                     190

Phe Gln Lys Glu Gly Ala Ala Gly Arg Asp Phe Ala
        195                     200

<210>  231
<211>  186
<212>  PRT
<213>  Homo sapiens

<400>  231

Gln Gly Arg Cys Thr Pro Pro Val Ile Leu Gly Val Ile Ser Ser Pro
1               5                   10                  15

Pro Leu Asp Ile Arg Asn Asn Ile Thr Ala Gly Val Gly Val Val Tyr
            20                  25                  30

Ser Leu Cys Asn Ile Gly Ser Asn Ile Ile Leu Ser Pro His Trp Ile
        35                  40                  45

Leu Gly Thr Ile Ser Gln Glu Val Trp Thr Pro Pro Ala Ile Leu Gly
    50                  55                  60

Val Thr Ser Phe Ser Phe Pro Ser Gly Tyr Glu Gln Tyr Cys Ile Gly
65                  70                  75                  80

Val Tyr Thr Pro Ser Asp Ile Arg Ser Asn Ile Ile Leu Ser His Ser
                85                  90                  95

Gly Tyr Glu Gln Tyr Leu Arg Arg Ser Val Glu Pro Leu Arg Tyr Glu
            100                 105                 110

Tyr His Pro Leu Pro Pro Trp Ile Leu Gly Thr Ile Thr Gln Gly Glu
        115                 120                 125
```

Tyr Thr Ala Pro Val Ile Leu Arg Val Ile Ser Ser Pro His Leu Asn
130 135 140

Ile Arg Asn Asn Ile Arg Gly Val Gly Tyr Thr Ile Cys Asp Ser Gly
145 150 155 160

Arg Asn Ile Ile Leu Ser Pro Pro Gly Tyr Glu Gln Tyr His Lys Trp
165 170 175

Ser Ile His Pro Leu Arg Tyr Trp Glu Tyr
180 185

<210> 232
<211> 157
<212> PRT
<213> Homo sapiens

<400> 232

Asp Asn Leu Cys Ser Pro Cys Ser Ser Thr Pro His Ile Pro Ile Val
1 5 10 15

Cys Pro Phe His Ser Ala Pro Phe Ser Val Gln Thr Glu Leu Phe Thr
20 25 30

Asn His Tyr Pro Leu Leu Glu Met Glu Gly Ala Pro Phe Pro Thr Pro
35 40 45

Pro Leu Pro Pro Gln Leu Ser Ser Pro Arg Arg Leu Ser Ile Asn Arg
50 55 60

Leu Thr Ile Ser Leu Asn Phe His Ile Phe Val Trp Leu Ser Tyr Leu
65 70 75 80

Phe Thr Phe Ile Asn Leu Leu Cys Phe Ser Leu Val Asn Gln Ser Phe
85 90 95

Phe Ile Gly Val Ser Ala Val Ser Leu Tyr Asp Gly Glu Glu Lys Asn
100 105 110

His Pro Leu Ser Thr Pro Thr Ser Asp Arg Ser Gln Asp Ile Pro Leu
115 120 125

Lys Phe Gly Lys Val Asn Thr Ser Thr Pro Cys Ile Leu Pro Asp Asn
130 135 140

Thr Lys Asn Phe Ile Gln Tyr Ile Tyr Tyr Met Ile Lys
145 150 155

<210> 233
<211> 178
<212> PRT
<213> Homo sapiens

<400> 233

Arg Ser Arg Lys Val Asn Trp Pro Lys Val Gly Ile Tyr Ile Pro Val
1 5 10 15

Leu Leu Leu Glu Cys Cys Leu Phe Leu Asn His Pro Trp Ser Arg Pro
20 25 30

Thr Pro Ser Cys Thr Tyr Thr Asn Pro Ile Leu Ser Gln Thr Gly Leu
35 40 45

```
Trp Leu Asp Ile Gly Glu Lys Gln Leu Asp Gly Leu Thr Pro Lys Lys
    50                  55                  60

Asn Pro Ala Arg Asp Gly Gln Asn Phe Arg Gly Gly Leu Arg Tyr Arg
65                  70                  75                  80

Pro Cys Leu Leu Leu Ser Ser Pro Ser Cys Arg Glu Pro Arg Phe Ile
                85                  90                  95

His Asn Lys Ile Pro His Ile His His Pro Ser Ile Tyr Ser Cys Asn
            100                 105                 110

Leu Ile Phe Pro Gly Trp Trp Thr Arg Ala Arg Glu Pro Gln Val Glu
        115                 120                 125

Ile Gln Lys Ala Val Thr Leu Ala Leu Cys Pro Cys Trp Arg Arg Ala
    130                 135                 140

Ala Ala Ser His Arg Gly Arg Gly Pro Thr Glu Leu Leu Thr Leu Lys
145                 150                 155                 160

Pro Ser Ala Asp Gly Arg Ala Lys Thr Ala Leu Glu His Ala Leu Trp
                165                 170                 175

Gly Phe


<210>  234
<211>  188
<212>  PRT
<213>  Homo sapiens

<400>  234

Ile Glu Thr Lys Leu Asn Thr Phe Ala Lys Leu Leu Arg Ser Lys Phe
1               5                   10                  15

Leu Val Pro Arg Leu Glu Leu Pro Asn Ala Asp Lys Ser Ser Pro Val
            20                  25                  30

Gly Ser Pro Thr Leu Phe Lys Gln Phe Leu Asp Phe Ala Pro Val Glu
        35                  40                  45

Ala Asp Met Leu Asn His Lys Thr Pro Leu Leu Leu Ala Leu Ala Tyr
    50                  55                  60

Cys Phe Gly Arg Ser His Phe Ser Lys Ile Arg Ala Ser Leu Ile Asn
65                  70                  75                  80

Thr Gly Ile Arg Phe Leu Ser Gly Val Gly Ile Pro Glu Asp Arg Ile
                85                  90                  95

Ile Tyr Phe Ala Leu Ser Arg Cys Val Met Arg Thr Glu Ala Met Leu
            100                 105                 110

Ile Arg Asp Pro Trp Glu Leu Val Ile Tyr Tyr Leu Leu Phe Leu Pro
        115                 120                 125

Lys Ile Asp Leu Met Glu Arg Gly Cys Ile Ile Tyr Pro Leu Ser Lys
    130                 135                 140

Glu Ala Phe Pro Asn Thr Thr Glu Ala Val Ile Leu Lys Thr Ala Leu
145                 150                 155                 160
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Trp Leu Cys Ser Gln Leu Tyr Phe Leu Pro Phe His Asn Phe Leu Pro
165 170 175

Ser Ala Met Glu Leu Met Gly His Thr His Ile His
180 185

<210> 235
<211> 165
<212> PRT
<213> Homo sapiens

<400> 235

Lys Lys Lys Thr Pro Met Ile Trp Ile Leu Leu Ser Phe Leu Phe Ser
1 5 10 15

Gln Met Val Ile Leu Lys Leu Ile Glu Val Val Tyr Arg Val His Ser
20 25 30

His Thr Val Arg Lys Arg Gln Ser Gln Gly Leu Asn Ser Ser Ser Leu
35 40 45

Thr Ile Glu Pro Ile Phe Leu Ile Thr Ile Gln Tyr Phe Thr Ile Cys
50 55 60

Ser Ile Lys Arg Asn His Phe Ser Glu Trp Arg Asn Ile His Glu Asn
65 70 75 80

Lys Ser Ile Ile Gln Asp Thr Cys Lys Ala Ser Arg His Ser Arg Phe
85 90 95

Arg Leu Leu Ala Pro Trp Pro Arg Leu Ile Thr Phe Gln Glu Asn Lys
100 105 110

Thr Thr Tyr Gln Asp His Thr Ser Arg Asn Asp Leu Arg Ile Met Gly
115 120 125

Thr Ala Ile Trp Val Ser Asn Gly Leu Glu Ser Asp Lys Trp Phe Leu
130 135 140

Asn Arg Phe Pro Glu Trp Gly Asn Leu Val Leu His Gln Ala Thr Tyr
145 150 155 160

Val Ile Phe Ile Leu
165

<210> 236
<211> 218
<212> PRT
<213> Homo sapiens

<400> 236

Ser Phe Leu Ser Phe Asn Arg Val Glu Lys Ile Ile Ile Ser Trp Glu
1 5 10 15

Pro Ser Phe Phe Tyr Tyr His Glu Cys Lys Cys Thr Ser Met Thr His
20 25 30

Leu Pro Leu Arg Ile Lys Leu Gln Tyr Lys Lys Tyr His Tyr Thr Tyr
35 40 45

Leu Ser Leu Ser Phe Asn Cys Leu Leu Glu Pro Ile Leu Phe Cys Leu
50 55 60

Pro Arg Thr Ser Thr Met Asp Tyr Pro Phe Thr Ile Ala Leu Ser Phe
65 70 75 80

Ser Ser Phe Cys Ile Cys Phe Pro Leu Ile Phe Lys His Asp Val Ile
85 90 95

Phe Ile Arg Asp Ile Asn Ile Leu Ile Thr Trp Phe Thr Arg Thr Thr
100 105 110

Pro Ser Ser Val Val Trp Arg Thr Lys Leu Leu Glu Arg Asp Val Gln
115 120 125

Thr Gln Tyr Leu Tyr Phe Cys Met Pro His Lys Ser Ser Leu Ile Phe
130 135 140

Ile Leu Ile Ser Leu Leu Lys Asp Val Thr Lys Asp Thr Asn Glu Phe
145 150 155 160

Gln Lys Ser Pro Asn Pro Met Glu Ile His Phe Pro Leu Ser Leu Ser
165 170 175

Ser Asn Ile Leu Pro Leu Val Phe Gln Asp Ser Phe Leu Leu Ser Phe
180 185 190

Leu Leu Thr Leu Phe Ser Ser Leu Lys Ile His Pro Pro Leu Pro Ser
195 200 205

His Lys Met Leu Arg Val Glu Gly Gly Ser
210 215

<210> 237
<211> 139
<212> PRT
<213> Homo sapiens

<400> 237

Thr Gln Cys Gln Phe Thr Lys Tyr Thr Ile Ile Tyr Ser Gln Asn Thr
1 5 10 15

Phe Ile Lys Arg Asn Phe Phe Lys Arg Arg Ser Cys Gln Cys Gln Tyr
20 25 30

Arg Asn Tyr Lys Asn Pro Phe Leu Phe Pro Leu Glu Ile Pro Ser Leu
35 40 45

Asp Cys Cys Ser Lys Asn Leu Ile Ser Lys Val Val Ser Leu Ser Leu
50 55 60

Asp Asn Asp Ile Arg Lys Cys Ser Arg Gln Ile Phe Ser Lys Ile Gln
65 70 75 80

Ser Ile Trp Tyr Leu Pro Lys Ser Lys Leu Gln Arg Glu Pro Glu Cys
85 90 95

Ser Pro Thr Ala Phe Ser Ser Ser Thr Gln Trp Ile Ser Tyr Met Leu
100 105 110

Asn Cys His Val Cys Ala Ser Leu Lys Cys Ala Phe Leu Phe Thr Glu
115 120 125

Met Arg Asp Val Leu Phe Met Ile Phe Ser Leu
130 135

<210> 238

<211> 213
<212> PRT
<213> Homo sapiens

<400> 238

Phe Gln Tyr Phe Val Thr Cys Arg Ser Lys Trp Trp His Ala Ser His
1 5 10 15

Leu Val Asn Ser Arg Ser Cys Cys Val Ser Asn Gly Asp Thr Leu Trp
20 25 30

Leu Leu Gln Met Val Thr Leu Pro Asn Cys Phe Pro Lys Arg His Val
35 40 45

Ala Phe Phe Ser Gln Ser Leu Ile Leu Thr Leu Met Val Ile Leu Leu
50 55 60

Tyr Phe Tyr Met His Leu Val Thr Cys Leu Ile Val Ile Phe Leu Glu
65 70 75 80

Ile Gln Phe Leu Leu His Arg Val Ser Phe Glu Ile Lys Glu Arg Glu
85 90 95

Val Ala Asn Leu Gly Cys Asn Asn Phe His Leu Lys Val Asp Pro Cys
100 105 110

Phe Tyr Tyr Pro Ile Ile Asn Val Phe Cys Phe Pro Leu Ser Ala Ser
115 120 125

Tyr Cys Ser Phe Asp Ser Tyr Cys Gln Thr Glu Leu Ser Cys Phe Leu
130 135 140

Ala Arg Lys Glu Thr Thr Met Asn Glu Pro Leu Asp Tyr Leu Ala Asn
145 150 155 160

Ala Ser Asp Phe Pro Asp Tyr Ala Ala Ala Phe Gly Asn Cys Thr Asp
165 170 175

Glu Asn Ile Pro Leu Lys Met His Tyr Leu Pro Val Ile Tyr Gly Ile
180 185 190

Ile Phe Leu Val Gly Phe Pro Gly Asn Ala Val Val Ile Ser Thr Tyr
195 200 205

Ile Phe Lys Met Arg
210

<210> 239
<211> 168
<212> PRT
<213> Homo sapiens

<400> 239

Trp Phe Thr Tyr Pro Leu Asn Lys Gln Leu Leu Arg Ile Pro Ala Pro
1 5 10 15

Ala Gln Arg Gln Tyr Trp Gly Leu Cys Leu Arg Met Trp Ala Leu Glu
20 25 30

Leu Cys Gly Trp Gly Ser Asn Ser Gly Arg Ala Ala Val Arg Pro Trp
35 40 45

Thr Ser Gly Ser Ser Lys Thr Asp Arg Gln Phe Ile Phe Ile Leu Val

50 55 60

Pro Gln Ile Val Val Leu Leu Ser Asn Tyr Leu Gly Phe Ile Pro Arg
65 70 75 80

His Trp Glu Ser Lys Leu Phe Ser Phe Ser Cys Leu Gln Lys Ser Ser
85 90 95

Leu Thr Ile His Val Ala Tyr His Trp Ile Gly Leu His Ile Lys His
100 105 110

Phe Val Thr Thr Phe Ala Cys Gly Tyr Ile Leu Leu Ser Phe Ser Tyr
115 120 125

Phe Leu Leu Ala Leu Leu Glu Tyr Ser His Lys Ser Leu Ser Ser His
130 135 140

Phe Trp Pro Pro Phe Asp Ser Phe Ser Leu Leu Cys Cys Cys Glu Ser
145 150 155 160

Phe His Val Gln Asp Ser Arg Trp
165

<210> 240
<211> 185
<212> PRT
<213> Homo sapiens

<400> 240

Ser Thr Met Cys Ile Phe Phe Trp Ala Lys Met Arg Gln Arg Cys His
1 5 10 15

Val Asn Phe Ser Phe Leu His Thr Thr Ile Val Ser His Lys Thr Lys
20 25 30

Asn Lys Arg Lys His Met Phe Thr Val Gly Arg Ile Ile Thr Arg Ser
35 40 45

Ser Val Ala Trp Pro Lys Glu Pro Leu Pro Thr Tyr Trp Gly Cys His
50 55 60

Met Lys Gly Phe Ser Lys Arg Leu Ala Ile Phe Ile Lys Gly Val Arg
65 70 75 80

His Gly Ser Gly Gln Gln Thr Ser Leu Trp Lys Gly Ser Lys Leu Leu
85 90 95

Gln Gln Asn Glu Arg Ile Met Val His Leu Pro Thr Leu Cys Asn Leu
100 105 110

Trp Met Lys Pro Gln Pro Arg Lys Val Lys Leu Leu Cys Val Cys Val
115 120 125

Trp Gly Cys Glu Gly Arg His Arg Lys Gly Lys Ala Asp Arg Pro Trp
130 135 140

Lys Thr Asp Ile Ser Pro Gly Glu Trp Asn Gly Gln Ser His Asn Thr
145 150 155 160

His Val Leu Asn Ile Thr Cys Phe Arg Lys Tyr Asn Ile Lys Thr Leu
165 170 175

Phe Lys Ser Tyr Ser Leu Met Ile Ser
180 185

<210> 241
<211> 196
<212> PRT
<213> Homo sapiens

<400> 241

Val Leu Asp Ile Asp Val Arg Met Gly Gly Leu Ser Tyr Pro Ser Pro
1 5 10 15

His Val Phe Leu Leu Arg Asp Ser Asn Cys Asn Thr Ser Leu Val Phe
20 25 30

Phe Ala Ser Ser Leu Ile Pro Tyr Gln Gly Lys Ser Ser Glu Leu Ser
35 40 45

Asn Glu Ile Trp Lys Glu Lys Val Ser Lys Tyr Thr Gln His Tyr Ser
50 55 60

Thr Ser Phe Ser Leu Gly Leu Ala Ser Leu Gln Arg Glu Tyr Ile Leu
65 70 75 80

Leu Cys Ala Gly Ser Phe Pro Lys Leu Ile Ser Gly Phe Val Asn His
85 90 95

Gly Thr Ile Asp Ile Leu Asp Gln Ile Ile Leu Cys Cys Met Ala Cys
100 105 110

Ser Val Phe Cys Gln Ile Phe Gly Ile Ile Pro Gly Leu Asn Leu Pro
115 120 125

Asp Ala Asn Ser Thr Phe Ser Leu Lys Thr Ile Glu Ile Phe Gln Asp
130 135 140

Val Ala Lys Cys Pro Ser Gly Leu Lys Val Ala Pro Asn Ser Asn His
145 150 155 160

Cys Phe Glu Ala Cys His His Arg Glu Gly Cys Leu Arg Leu Asn Val
165 170 175

Cys Leu Arg Leu Ile Tyr Thr Pro Lys Ser Asn Ser Thr Val Thr Leu
180 185 190

Ile Ser Arg Lys
195

<210> 242
<211> 198
<212> PRT
<213> Homo sapiens

<400> 242

Phe Ala Leu Phe Pro Met Phe Ile Ile Ser Leu Asn Gly Thr Pro Ile
1 5 10 15

Cys Met Val Ala Trp Glu Ile Tyr Gly Ile Ile Leu Glu Pro Ser Phe
20 25 30

Phe Ile Ile Pro Met Ser Arg Ser Glu Ile Leu Ser Glu Tyr Ala Ser
35 40 45

Leu Ile Tyr Leu Lys Leu Ala His Phe Lys Phe Leu Ser Ile Leu Thr
50 55 60

```
Leu Leu Tyr Leu Asn Asp Tyr His Ser Pro Asn Cys Phe Leu Met Gly
65                  70                  75                  80

Leu Ile Gly Lys Thr Asn Leu Phe Leu Ile Leu Pro Leu Glu Leu Ser
                85                  90                  95

Phe Gln Thr Arg Met Trp Pro Ser Phe Phe Leu Thr Asn Asp Leu Ile
            100                 105                 110

Val Pro Lys Thr Lys Ser Ile Leu Ser Leu Asn Asn Ile Gln Gly Pro
        115                 120                 125

His Ser Arg Ser Ser Leu Ile Pro Thr Ser Val Phe Leu Ser Ser Ser
    130                 135                 140

Pro Ser Gln Ser Thr Leu Ser His Thr Arg Tyr Ser Thr Trp Ser His
145                 150                 155                 160

Ile Lys Leu Leu Ser Ile Leu Gly Phe Leu Leu Ala Phe Asn Pro Leu
                165                 170                 175

Leu Gly Trp Cys Ile Pro Gly Glu Trp Ser Asn Pro Cys Thr Cys Tyr
            180                 185                 190

His Ala Pro Thr Phe Leu
        195

<210>  243
<211>  180
<212>  PRT
<213>  Homo sapiens

<400>  243

Leu Cys Asp Gly Val Met Arg Trp Gly Arg Arg Val Trp His His Ala
1               5                   10                  15

Thr Gly Phe Pro Pro Lys Leu Ser Thr Pro Arg Ser Thr Ser Ala Ser
            20                  25                  30

Gly Met Ser Ala Gly Ser Gln Arg Leu Trp Arg Arg Gly Ser Ser His
        35                  40                  45

Ala Val Gln Thr Phe Asn Pro Leu Gln Ser Ser Leu Ala Arg Glu Gln
    50                  55                  60

Gln Ser Leu Leu Glu Arg Asn Tyr His Ser Lys Gln Glu Phe Arg Pro
65                  70                  75                  80

His Leu Ser Glu Asp His Val Glu Val His Leu Ala Gly Lys Val Ala
                85                  90                  95

Ser Gly Cys Gly Leu Phe Asn Tyr Thr Leu Leu Phe Thr Leu Phe Thr
            100                 105                 110

Ile Val Cys Lys Val Gln His Leu Gln Ala Arg Asn Thr Gly Leu Pro
        115                 120                 125

His Ser Gly Trp Leu Gly Leu Met Lys Ala Ala Lys Gln Cys Ala Gln
    130                 135                 140

Ser Lys Gln Arg Leu Pro Leu Ala Gly Ala His Ser Pro Arg Glu Gly
145                 150                 155                 160
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Ile Ser Phe Ser Leu Asp Leu Gly Ala Lys Ala Thr His Gly Ser Asp
165 170 175

Gln Thr Thr Cys
180

<210> 244
<211> 129
<212> PRT
<213> Homo sapiens

<400> 244

Val Glu Gln Leu Glu Thr His Gly Ser Val Leu Glu Trp Leu Val Trp
1 5 10 15

Asp His Phe Leu Gly Asp His Ser Ala Leu Thr Asp Gln Thr Gln Val
20 25 30

Asn Gly Thr Cys Pro Leu Pro Phe Pro Pro Gly Phe Gly Thr Val Ala
35 40 45

Thr Arg Val Val Phe Pro Ser Arg Gln Leu Leu Arg Val Ile Pro Glu
50 55 60

His Ser Leu Gly Ala Cys Ser Val Leu Thr Val Ile Ser Phe Ile Leu
65 70 75 80

Thr Ala Ile Pro Phe Cys Ile Phe Ser Gly His Pro Gln Asp His Pro
85 90 95

Gly Gln Pro Cys Leu Thr Pro Gly Leu Val Trp Leu His Asp Asn Lys
100 105 110

Asp Ala Gly Pro Glu Thr Ile Pro Leu His Gly Ala Cys Ile Phe Pro
115 120 125

Leu

<210> 245
<211> 181
<212> PRT
<213> Homo sapiens

<400> 245

Glu Ser Lys Met Leu Ile Gly Gly Ala Pro Pro Gln Cys Val Glu Asp
1 5 10 15

Leu Ala Ala Leu Asp Ala Tyr Ser Gln Ala Leu Gly Thr Arg Glu Ala
20 25 30

Pro Gly Leu Pro Phe Trp Ala Val Asp Leu Trp Gly Arg Ser Trp Pro
35 40 45

Leu Gly Trp Cys His Cys Ser Ser Tyr Pro Lys Cys Pro Phe Tyr Ala
50 55 60

Cys Ser Gly Leu Ala Ser Asn Thr Leu Lys Val Ser Ser Lys Gly Gln
65 70 75 80

Gly Arg Val Pro Cys Gly Lys Arg Trp Leu Phe Glu Ala Lys Ala Gln
85 90 95

Arg Arg His Ser Gln Arg Met Gly Arg Ala Ala Gly Gln Val Ser Ala
100 105 110

Ser Thr Trp Lys Thr Pro Ala Trp Leu Ala Ala Gly Glu Ile Val Leu
115 120 125

Pro Arg Cys Gln Leu Leu Ser Arg Pro Leu Pro Arg Glu Pro Ser His
130 135 140

Leu Ser Phe Ser Tyr Pro Ser Leu Arg Lys Ala Gln Ala Gln Gly Ala
145 150 155 160

Met Val Pro Cys Ser Gln Thr Val Ile Ser Glu Trp Pro Leu Val Trp
165 170 175

Gly Pro Arg Val Gln
180

<210> 246
<211> 137
<212> PRT
<213> Homo sapiens

<400> 246

Gln Asn Thr Phe Tyr His Ile Asn Ser Cys Thr Met Ile Trp Leu Glu
1 5 10 15

Glu Lys Asn Ser Trp Lys Val Lys Phe Val Leu Lys His Leu Phe Lys
20 25 30

Ser Leu His Thr Phe Ile Cys Pro Asp Lys Thr Cys Leu Asn Phe Phe
35 40 45

Leu Lys Gln Leu Tyr Cys Pro Ser Ile Cys Leu Thr Lys Phe Phe Lys
50 55 60

Gly His Phe Gln Pro Phe Gln Arg His Lys Val Gly Val Pro Lys Pro
65 70 75 80

Pro Phe Leu Ala Leu Pro Val Glu Asn Thr Met Leu His Ser Tyr Met
85 90 95

Cys Pro Leu Thr Gln Thr Thr Leu Ile Leu Arg Arg Ser Leu Asp Leu
100 105 110

Lys Leu Leu Leu Leu Ala Val Pro Ala Asn Ser Arg Val Lys Glu Asp
115 120 125

Val Thr Arg His Thr Tyr Leu Pro Phe
130 135

<210> 247
<211> 149
<212> PRT
<213> Homo sapiens

<400> 247

Ser Pro Met Leu Gln Phe Tyr Arg Leu Gly Lys Leu Arg Ala Gly Val
1 5 10 15

Thr Cys Tyr Ser Ser Tyr Pro Gln Thr Tyr Lys Thr Lys Ser Phe Thr
20 25 30

Glu Val Lys Tyr Asn Leu Phe Gly Leu Leu Phe His Phe Thr Ile Leu
35 40 45

Ser Leu Leu Val Phe Ile Thr Ile His Ser Lys Glu Phe Ile His Val
50 55 60

Asp Thr Ser Glu Val Phe Leu Ile Ser Pro Val Arg Pro Val Val Lys
65 70 75 80

Leu Leu Trp His Tyr Ser Thr Phe Ser Leu Ser Val Phe Phe Pro Ser
85 90 95

Pro His Arg Ser Glu Leu Ile Ser Pro His Pro Gly Pro Ser Glu Ser
100 105 110

Phe Val Lys Ser Leu Leu Ser Asn Leu Ser Val Glu Arg Val Pro Leu
115 120 125

Cys Leu Ser Glu Ile His Thr Val Met Cys His Leu Thr Met Phe Gln
130 135 140

Ser Val Arg Asp His
145

<210> 248
<211> 145
<212> PRT
<213> Homo sapiens

<400> 248

Pro Ile Pro Pro Ser Glu Gly Leu Glu Lys Ala Phe Thr Phe Met Ser
1 5 10 15

Pro Gly Ile Arg Ser Pro Gln Thr Arg Asn Phe Phe Leu Ile Met Glu
20 25 30

Val Trp Gln Trp Ala Thr Lys Pro Lys Val Ser Val Leu Leu Ser Asp
35 40 45

Ile Ala Ser Leu Arg Asn Arg Gln Pro Gly Arg Asp Gly Met Ser Leu
50 55 60

Ile Lys Cys Ser Ala Glu Val Ser Ser Arg Gly Leu Trp Cys Cys Pro
65 70 75 80

Ser Gly Cys Asn Ile Cys Thr Lys Pro Val Thr Glu Tyr Tyr Thr Glu
85 90 95

Ser Val Val Pro Lys Ile His Gly Phe Leu Tyr Gln Gly Leu Asp Ile
100 105 110

Glu Ser Ala Leu Val Thr Ile Lys Trp Leu Arg Asn Phe Tyr Phe Ile
115 120 125

Cys Pro Gln Leu Arg Trp Ile Arg Ser Val Cys Ile Leu Ala Ser Val
130 135 140

Cys
145

<210> 249
<211> 146
<212> PRT
<213> Homo sapiens

<400> 249

Leu Thr Ser Val Ser Ser Val Lys Pro Lys Leu Ser Lys Cys Glu Ile
1 5 10 15

Met Lys Cys Val Lys Leu Leu Ile Gln Cys Leu Arg Gln Gln Asn Ser
20 25 30

Arg Leu Ile Ile Gln Ser Ile Gln Thr Thr Phe Tyr Gly Asp Asn Leu
35 40 45

Trp Ser Glu Arg Leu His Lys Cys Ser Phe His Ser Tyr Ser Ser Ser
50 55 60

Asn Thr Lys Leu Leu Ser Ile Pro Glu Leu Lys Met Thr Leu Leu Thr
65 70 75 80

Asp Leu Tyr Leu Phe Ile Cys His Phe Ser Arg Arg Thr Ala Ile Leu
85 90 95

Pro Gln Ser Pro Tyr Ala Phe Val Glu Ser Trp Leu Lys Pro Gln Ala
100 105 110

Leu Cys Lys Ala Phe Leu Gly Ile Asp Ile Thr Thr Ile Pro Gln Asn
115 120 125

Leu Leu Val Leu His Ala Ile Ser Gly Pro Trp Thr His Phe Tyr Cys
130 135 140

Asn Lys
145

<210> 250
<211> 84
<212> PRT
<213> Homo sapiens

<400> 250

Phe Thr Gln Glu Ser Ser Arg Pro Ser Thr Phe Gly Ala Asn Leu Glu
1 5 10 15

Leu Gly Cys Arg Pro Ala Gly Thr Phe Ile Lys Cys Tyr Tyr Phe Ile
20 25 30

Phe Ala Ser Glu Glu Leu Pro Asp Phe Val Lys Thr Leu Cys Asn Pro
35 40 45

Ser Pro Phe Phe Trp His Ser Arg Gln Leu Asn Lys His Leu Leu Thr
50 55 60

Pro Leu Leu Cys Val Ile Arg Cys Glu Arg His Trp Arg Tyr Glu Glu
65 70 75 80

Pro Met Val Ser

<210> 251
<211> 62
<212> PRT
<213> Homo sapiens

<400> 251

Ala Pro Trp Gly Trp Ala Ser Val Ser Val Cys Ala Arg Leu Glu Met
1   5   10   15

Ala Ser Arg Tyr Gly Leu Gln Glu His His Glu Val His Leu Ile Phe
            20   25   30

Ala Phe Leu Cys Gln His Val Cys His Leu Gln Cys Leu Thr Glu His
        35   40   45

Val Gly Pro Ala Met Trp Ala Val Ser Leu Pro Ser Ser Tyr
    50   55   60

<210> 252
<211> 117
<212> PRT
<213> Homo sapiens

<400> 252

Lys Lys Glu Pro Thr Met Ile Trp Ile Leu Leu Ser Phe Leu Phe Ser
1   5   10   15

Gln Met Val Ile Leu Lys Leu Ile Glu Val Val Tyr Arg Val His Ser
            20   25   30

His Thr Val Arg Lys Arg Gln Ser Gln Gly Leu Asn Ser Ser Ser Leu
        35   40   45

Thr Ile Glu Pro Ile Phe Leu Ile Thr Ile Gln Tyr Phe Pro Ile Cys
    50   55   60

Ser Ile Lys Arg Asn His Phe Ser Glu Trp Arg Asn Ile His Glu Asn
65   70   75   80

Lys Ser Ile Ile Gln Asp Thr Cys Lys Ala Ser Arg His Ser Arg Phe
                85   90   95

Arg Leu Leu Ala Pro Trp Pro Arg Leu Ile Thr Phe Gln Glu Asn Lys
            100   105   110

Thr Thr Tyr Gln Asp
        115

<210> 253
<211> 134
<212> PRT
<213> Homo sapiens

<400> 253

Thr Phe Ile Lys His Phe Phe Ser Gly Leu Ser Phe Ser Pro Ser Cys
1   5   10   15

His Val Ala Ile Ile Ile Phe Thr Ser Ala Ser Ala Tyr Phe Lys Pro
            20   25   30

His Asn Lys Leu Leu Ala Phe Phe Phe Ala Ile Asp Asn Asn Leu Lys
        35   40   45

Met Thr Gln Asn Phe Asn Gly Phe Ile Tyr Pro Gln Phe Tyr Asp Phe
    50   55   60

Arg Ser Ser Phe Leu Cys Val Asp Leu Leu Ile Tyr His Phe Leu Ser
65   70   75   80

Thr Ile Thr Ser Phe Asn Leu Ser Cys Ser Thr Gly Leu Leu Thr Ile
85 90 95

Asn Phe Phe Ser Phe Ser Leu Ser Lys Asn His Leu Phe Ser Leu His
100 105 110

Phe Cys Lys Ile Phe Ser Arg Val Ile Lys Phe Val Thr Ile Phe Phe
115 120 125

Glu Tyr Phe Lys Asp Leu
130

<210> 254
<211> 138
<212> PRT
<213> Homo sapiens

<400> 254

Thr Phe Leu Ser Arg His Phe Leu Met Trp Lys Arg Phe Thr Glu Ser
1 5 10 15

Asp Thr Phe Lys Gly Leu Thr Arg Asp Ile Cys Cys Leu Cys Leu Leu
20 25 30

Phe Ser Trp Arg Ser Ala Thr Asn Lys Ala Ser Ser Thr Gln Gly His
35 40 45

Leu Ser Thr Gly Leu Phe Leu Ser Ser Ser His Asn Leu Ser Cys His
50 55 60

Thr Ile Thr Ser Thr Thr Ser Leu Gly Pro Cys Ser Glu Pro Thr Phe
65 70 75 80

Phe Leu Pro Gln Val Gly Ile Ala Ser Ala Pro Tyr Cys Leu His Ser
85 90 95

Glu Gly Ser Tyr Val His Ala Leu Asn Lys Phe Val Ser Pro Ile Asn
100 105 110

Val Pro Phe Ala Ser Phe Phe Ser Glu Thr Ser Glu Val Gln Arg Gln
115 120 125

Pro Leu Pro Ser Ser Arg Cys Ser Thr Tyr
130 135

<210> 255
<211> 155
<212> PRT
<213> Homo sapiens

<400> 255

Cys Lys Thr Gly Gly Leu Lys Leu Ile Phe Arg His His Gly Ile Leu
1 5 10 15

Tyr Arg Leu Ser Leu Tyr Leu Glu Asp Val Arg Leu Met Glu Val Leu
20 25 30

Ser Ile Leu Phe Pro Leu Leu Ile His Ser Phe Leu Phe Thr Glu Arg
35 40 45

Leu Asn Phe Leu Ser His Ile Ser Val Leu Leu Ala Pro Leu Phe Phe
50 55 60

Pro Leu Leu Gln Lys Ser Gln Pro Gln Lys Gln Ser Thr Tyr Cys Glu
65 70 75 80

Lys Asp Phe Ser Asn His Lys Gly Asp Val Thr Leu Gly Leu Cys Phe
85 90 95

Leu Ser His Thr His Lys Ile Leu Asp Met Ser Glu Ile Leu Lys Asn
100 105 110

Trp Phe Leu Asn Val Met Lys Arg Val Ser Phe Ser Pro Glu Gln Asn
115 120 125

Asn Pro Cys Ser Leu Leu Pro Asp Met Gly Gly Phe Gln Ile Arg Asn
130 135 140

Leu Cys Ile Gly Pro Gln Ala Pro Asp Lys Val
145 150 155

<210> 256
<211> 185
<212> PRT
<213> Homo sapiens

<400> 256

Gly His Arg Pro Ser Phe His Phe Cys Lys Pro Arg Gly Ile Leu Thr
1 5 10 15

Asp Ser Thr Thr Tyr Pro Leu Leu Val Leu Ile Glu Glu Asp Thr Gly
20 25 30

Leu Lys Pro His Phe Phe Arg Ala Phe Val Cys Ile Ser Lys Ile Leu
35 40 45

Phe Tyr Arg His Leu Pro Phe Ser Phe Ile Phe Phe Leu Ser His Asn
50 55 60

Asn Ser Ala Phe Leu Leu Tyr Glu Cys Thr Ser Asp Leu Thr Gln Arg
65 70 75 80

Ile Gly Gly Gln Thr Asp Cys Leu Leu Ser Val Ser Cys Ala Leu Leu
85 90 95

Arg Arg Leu His Leu Ser Ala Asn Ser Ser Cys Thr Thr Phe Ser Asp
100 105 110

Phe Cys Cys Val Phe Ser Asp His Leu Leu Gly Ser Gly His Pro Leu
115 120 125

Asp Gly Ser Gly Leu Ser Val Ser Val Phe Gly Asn Trp Ser Asp Leu
130 135 140

Ala Leu Leu Met Gln Leu Lys Leu Arg Pro Leu Ser Leu Ser Gln Ala
145 150 155 160

His Ser Gly Cys Val Arg Phe Leu Leu Ser Leu Val Cys Ile His Pro
165 170 175

Leu His Val Gln Val Gly Ala Ala Lys
180 185

<210> 257
<211> 128
<212> PRT
<213> Homo sapiens

<400> 257

His Phe Leu Pro His Ile Leu Glu Leu Val Leu Phe Leu Ile Lys Ile
1 5 10 15

Asn Val Ile Phe Arg Gly Ala Ile Phe Cys Phe Gln Asp Phe Phe Lys
20 25 30

Glu Val Ile Leu Lys Ala Lys Phe Lys Glu Lys Glu Leu Val Ala Leu
35 40 45

Val Asp Pro Val Gly Ser Ser Phe Leu Cys Trp Ser Ile Phe Cys Ile
50 55 60

Pro Phe Glu Phe Ala Phe Leu Phe Asn Ile Phe Trp Tyr Ser Arg Phe
65 70 75 80

Leu Phe Phe Gly Thr Phe Val His Ile Asn Phe Leu Val Trp Arg Arg
85 90 95

Gly Ile Leu Ile Ala Asn Gly Thr Lys Val Tyr Arg Asp Ile Val Gln
100 105 110

Pro Leu Leu Phe Phe Leu Phe Leu His Ser Ile Leu Val Met Gly Asn
115 120 125

<210> 258
<211> 168
<212> PRT
<213> Homo sapiens

<400> 258

Lys Gln Ser Tyr Ile Cys Ile Leu Phe Tyr Ile Tyr Phe Val Ile Phe
1 5 10 15

Leu Leu Ser Thr Val Ser Ser Leu Leu Pro Phe Leu Ile Glu Glu Phe
20 25 30

Asn Ala Cys Ile Cys Val Phe Ala Lys Lys Thr Pro Ser Ile Thr Cys
35 40 45

Ser Ile Tyr Glu Tyr Phe Trp Pro Leu Thr Gln Lys Val Leu Tyr Tyr
50 55 60

Arg Gln Lys Ser Thr Arg Lys Gln Ser Gly Thr Ser Ser Lys Arg Asp
65 70 75 80

Ser Ile Val Gly Lys Asn Thr Asp Pro Gly Gly Lys Leu Pro Gly Leu
85 90 95

Glu Ser Gln Leu Tyr Tyr Phe Gly Lys Thr Thr Tyr Leu Leu Tyr Leu
100 105 110

Phe Trp Tyr Pro Cys Leu Asn Gly Ser Asn Asn Asn Pro Leu Ile Ala
115 120 125

Leu Leu Gly Phe Asn Arg Ser Glu Asp Phe Arg Arg Ala His Asp Lys
130 135 140

Asn Tyr Ile Arg Val Thr Tyr Tyr Cys Tyr Pro Ile Cys His Ser Lys
145 150 155 160

Leu Arg Asp Leu Gly Gln Val Thr

165

<210> 259
<211> 182
<212> PRT
<213> Homo sapiens

<400> 259

Leu Val Glu Trp Ala His Ser Ser Met Arg Pro Ile Phe His Leu Asn
1 5 10 15

Phe Leu Cys Leu Arg Asn Glu Leu Tyr Ser Asn Leu Cys Phe Leu Lys
20 25 30

Ile Asn Val Phe Leu Val Lys His Leu Val Ser Ser Gln Ile Leu Phe
35 40 45

Lys Lys Thr Thr Glu Asn Ser Glu Glu Gly Glu Thr Asp Ser Ala Asn
50 55 60

Ser Ile Ser Val Pro Arg Leu Asn Trp Glu Met Leu Leu Leu His Asp
65 70 75 80

Leu Gly Leu Ile Ile Cys Leu Gln Glu His Cys Phe Arg Val Val Trp
85 90 95

Tyr Ser Gly Arg Asn Gly Leu Trp Ser Glu Ile His Val Gln Ile Pro
100 105 110

Ser His Leu Pro Ser Leu Ile Leu Ser Phe Leu Ile Cys Lys Met Thr
115 120 125

Ile Ile Asn Thr Ile Ser Lys Ile Cys Gly Asp Asn Thr Ala Phe Thr
130 135 140

Ser Cys Cys Ile Leu Pro Ile Ser Ser Cys Arg Asp Arg Ile Phe His
145 150 155 160

Phe Ile Leu Ile Tyr Asn Tyr Val Ile Pro Phe Lys Asn His Pro Ser
165 170 175

Thr Phe Ser Ser Thr Arg
180

<210> 260
<211> 207
<212> PRT
<213> Homo sapiens

<400> 260

Cys Ser Leu Leu Asp Phe Leu Met Leu Val Gly Ala Leu Arg Lys Leu
1 5 10 15

Cys Thr Lys Leu Asp Pro Val Leu Gln Gly Ser Asp Leu Thr Glu His
20 25 30

Ser Ala Trp Gly Val Pro Leu Ile Trp Thr Trp Asn Ser Ile Ile Gln
35 40 45

Arg Pro Ser Leu Pro Cys Ser Leu Cys Val Thr Gly Ala Ala Glu Thr
50 55 60

Gln Val Leu Ser Ala Ser Ala Gly Leu Gln Pro Cys Leu Cys Leu Leu

65 70 75 80

Arg Ser Asp Ser Asn Cys Tyr Leu Trp Arg Trp Leu Phe Ile Gly Thr
85 90 95

Pro Phe Leu Cys Leu Thr Glu Ala Gln Cys Ser Lys Leu Glu Gly Leu
100 105 110

Cys Gln His Val Ser His Thr His Leu Leu Leu Phe Phe Ser Arg Val
115 120 125

Leu Gly His Leu Leu Leu His Ile Thr Thr Ser Ser Pro Pro Ala Gln
130 135 140

Leu Ala Leu Ser Pro Phe Pro Ile Tyr His Ala Val Leu Glu His Lys
145 150 155 160

Ala Leu Leu Cys Ile Pro Cys Val Tyr Phe Val Val Met Cys Cys Ile
165 170 175

Leu Lys Glu Leu Asn Leu Cys Pro Gly Ser Arg Lys Asn Ala Asp Gln
180 185 190

Leu Leu Ala Ile Asp Gly Phe Asn Ile Ser Tyr Asp Trp Phe Leu
195 200 205

<210> 261
<211> 187
<212> PRT
<213> Homo sapiens

<400> 261

Gln Thr Lys Glu Glu Lys Gly Gln Val Lys His Thr Ile Gly Phe Thr
1 5 10 15

Val Asn Met Ser Lys Val Leu Leu Ile Ile His Phe Met Tyr Pro Arg
20 25 30

Leu Trp Lys Lys Phe Phe Phe His Leu Pro Ile Lys Asn Ile His Leu
35 40 45

Gly Ile Thr Thr Ser Trp Ile Leu Leu Asp Arg His Thr Thr Thr Leu
50 55 60

Thr Val Leu Pro Ser Ser Arg Arg Leu Ala Arg Lys Ala His His Pro
65 70 75 80

Leu Pro Gly Ser Lys Val Asp Ser Leu Ile Phe Cys Ile Asn Pro Thr
85 90 95

Pro Asp Ser Phe Ser Tyr Ser Leu Leu Pro Cys Leu Phe Ser Tyr Leu
100 105 110

Met Val Asn Val Phe Leu Ser Ser Cys Ile Thr Phe Tyr Ser Phe Leu
115 120 125

Glu His Ile Ile Ile Ile Asn Lys Lys Ser Lys Ile Ala Met Val Ala
130 135 140

Arg Ile Pro Ala Pro Leu Asp Pro Ser Thr Ser Ser Ser Pro Gly His
145 150 155 160

Thr Trp Gln Arg Glu Ile Lys Val Leu Asp Gly Ile Lys Val Asn Gln
165 170 175

Leu Thr Leu Lys Gly Glu Lys Glu Ser Arg Leu
180 185

<210> 262
<211> 149
<212> PRT
<213> Homo sapiens

<400> 262

Tyr Val Thr Ile Leu Leu Thr Val Leu Val Phe Leu Leu Arg Ser Leu
1 5 10 15

Pro Phe Gly Ile Arg Trp Ala Leu Ser Thr Gly Ile His Leu Asp Leu
20 25 30

Glu Val Ile Phe Cys His Val His Leu Val Ser Ile Phe Leu Ser Pro
35 40 45

Leu Asn Gly Ser Ala Asn Pro Val Ile Tyr Phe Phe Val Gly Ser Phe
50 55 60

Arg Gln Arg Gln Asn Arg Gln Asn Leu Lys Leu Val Leu Gln Arg Ala
65 70 75 80

Leu Gln Asp Met Pro Glu Val Lys Val Glu Gly Gly Phe Leu Arg Glu
85 90 95

Pro Trp Ser Cys Arg Glu Ala Asp Ser Gly Ser Glu Glu Glu Pro Leu
100 105 110

Pro Cys Gln Ser Asp Gly Thr Leu Arg Ala Ile Leu Pro Cys His Ala
115 120 125

Gln Leu His Ala Phe Ser Cys Cys Ala Ser Glu Met Ser Gln Arg Leu
130 135 140

Lys Val Val Glu Met
145

<210> 263
<211> 207
<212> PRT
<213> Homo sapiens

<400> 263

His Trp Arg Ser Leu Val Thr Trp Ala Glu Tyr Leu Glu Pro Arg Ile
1 5 10 15

Ser Ser Ser Met Val Asp Gln Leu Cys Asp Gly Val Met Arg Trp Gly
20 25 30

Arg Arg Val Trp His His Ala Thr Gly Phe Pro Pro Lys Leu Ser Thr
35 40 45

Pro Arg Ser Thr Ser Ala Ser Gly Met Ser Ala Gly Ser Gln Arg Leu
50 55 60

Trp Arg Arg Gly Ser Ser His Ala Val Gln Ser Phe Asn Pro Leu Gln
65 70 75 80

Ser Ser Leu Ala Arg Glu Gln Gln Ser Leu Leu Glu Arg Asn Tyr His
85 90 95

```
Ser Lys Gln Glu Phe Arg Pro His Leu Ser Glu Asp His Val Glu Val
            100                 105                 110

His Leu Ala Gly Lys Val Ala Ser Gly Cys Gly Leu Phe Asn Tyr Thr
        115                 120                 125

Leu Leu Phe Thr Leu Phe Thr Ile Val Cys Lys Val Gln His Leu Gln
    130                 135                 140

Ala Arg Asn Thr Gly Leu Pro His Ser Gly Trp Leu Gly Leu Met Lys
145                 150                 155                 160

Ala Thr Lys Gln Cys Ala Gln Ser Lys Gln Arg Leu Pro Leu Ala Gly
                165                 170                 175

Ala His Ser Pro Arg Glu Gly Ile Ser Phe Ser Leu Asp Leu Gly Ala
            180                 185                 190

Lys Ala Thr His Gly Ser Asp Gln Thr Thr Cys Ser Pro His Leu
        195                 200                 205

<210>  264
<211>  204
<212>  PRT
<213>  Homo sapiens

<400>  264

Gly Ala Ser Ser Gln Tyr Gly Asn Glu Asp Gly Val Asn Leu Phe Pro
1               5                   10                  15

Leu Met Ser Pro Pro Leu Tyr Thr Asn Leu Leu Lys Pro Thr Gly Lys
            20                  25                  30

Leu Arg Leu Gly Asn Lys Asn Ile Lys Cys Tyr Val Gln Ile Leu Lys
        35                  40                  45

Trp Asn Leu Lys Leu Leu Val Leu Gln Leu Phe Leu Lys Ile Pro Thr
    50                  55                  60

Leu Ser Arg Ser Met Ser Phe Arg Glu Arg Thr Tyr Val Ala Arg Glu
65                  70                  75                  80

Lys Ser Lys Glu Ser Met Asn Pro Val Leu Leu Ser Ile Leu Gln Cys
                85                  90                  95

Trp Arg Pro Phe Ser Ile Phe His Ser Leu Gly Gln Ser Phe Asn Thr
            100                 105                 110

His Leu Leu Lys Ala Ile Tyr Ile Arg Pro Cys Tyr Ser Lys Gly Thr
        115                 120                 125

Val Gly Gly Glu Glu Arg Gln Asp Pro Thr Met Glu Leu Lys Ser Ser
    130                 135                 140

Leu Asp Arg Phe Pro Phe Pro Ser Gly Gln Ser Lys Pro Asn Asp Thr
145                 150                 155                 160

Thr Val Ser Ser Phe Pro Glu Gln Arg Asp Val Glu Asn Tyr Leu Phe
                165                 170                 175

Thr Ile Val Arg Arg Arg Gln Gly Trp Asn Phe Phe Gln Asn Lys Leu
            180                 185                 190
```

Phe Phe Phe Val Lys Gln Gly Lys Ile Leu Leu Leu
195 200

<210> 265
<211> 186
<212> PRT
<213> Homo sapiens

<400> 265

Ile Ser Val Thr Asp Leu Ile Gly Gly Lys Trp Ile Phe Gly His Phe
1 5 10 15

Phe Cys Asn Val Phe Ser Val Asn Val Met Cys Cys Thr Ala Trp Ile
20 25 30

Leu Thr Leu Tyr Val Ile Ser Ile Asp Arg Tyr Leu Gly Ile Met Lys
35 40 45

Pro Leu Thr Tyr Pro Met Arg Gln Lys Gly Lys Cys Met Thr Lys Met
50 55 60

Ile Leu Ser Val Cys Leu Leu Ser Ala Phe Val Thr Leu Pro Thr Ile
65 70 75 80

Phe Gly Arg Ala Gln Asn Val Asn Asp Asp Lys Val Cys Leu Val Ser
85 90 95

Gln Asp Phe Gly Tyr Thr Ile Tyr Ser Thr Ala Leu Ala Ser Ser Pro
100 105 110

Cys Ala Ser Cys Phe Ser Cys Thr Asn Arg Phe Thr Arg Pro Pro Gly
115 120 125

Lys Ala Arg Pro Asn Thr Gly Tyr Leu Ala Ser Leu Glu Trp Ser Gln
130 135 140

Thr Ala Val Val Thr Leu Asn Gly Thr Val Lys Phe Gln Glu Val Glu
145 150 155 160

Glu Cys Ala Lys Leu Ser Arg Leu Leu Lys His Glu Arg Lys Lys Tyr
165 170 175

Leu His Leu Ala Glu Thr Glu Ser Ser Asp
180 185

<210> 266
<211> 184
<212> PRT
<213> Homo sapiens

<400> 266

Phe Thr Val Ile Asn Val Cys Ser Cys Thr Cys Glu Val Lys Ser Phe
1 5 10 15

Ser Leu Leu Ser Asn Ser Tyr Val Pro Asn Ile Phe Ser Lys Phe Leu
20 25 30

Lys Thr Tyr Asn Gly Glu Lys Asn Asn Pro Phe Ser Ser Pro Ala Ser
35 40 45

Leu Met Lys Asn Ser His Phe Ser Leu Phe Leu Leu Phe Leu Leu Val
50 55 60

Val Phe His Ile Ser Cys Leu Ser Ala Val Ser Cys Phe Met Gln Phe
65 70 75 80

Arg Pro Tyr Leu Leu Thr Ser Leu Ser Phe Gln Tyr Lys Asp Ser Cys
85 90 95

Ile Phe Ser Phe Asn Phe Thr Phe Leu Asn Ser Pro Phe Pro Phe Cys
100 105 110

Asp Pro Gly Ile Ser Gly Val Leu Phe Phe Phe Ile Leu Pro Asp Phe
115 120 125

Ile Tyr Ile Cys Val Tyr Ser Phe Leu Leu Phe Phe Lys Leu Lys Thr
130 135 140

Cys Leu Ser Ser Lys Ser Gly Ser Phe Phe Phe Ser Trp Arg Pro Leu
145 150 155 160

Ser Gln Asn Pro Leu Ser Phe Cys Phe Asn Glu Asp Tyr Met Leu Ser
165 170 175

Leu Trp Leu Pro Ser Cys Asn Thr
180

<210> 267
<211> 201
<212> PRT
<213> Homo sapiens

<400> 267

Phe Pro Ser Leu Lys Asn Met His Phe Ser Val Pro Leu Arg Cys His
1 5 10 15

Thr Ile Ile Ser Val Gln Lys Arg Val Asn Thr Ala Asp Pro Arg Leu
20 25 30

Leu Leu Leu Lys Cys Pro Ala Cys Lys Ala Gly Ser Trp Leu Val Phe
35 40 45

Gly Val Leu Asp Phe Glu Lys Leu Pro Thr Ile Pro Ser Thr Gly Leu
50 55 60

Cys Lys Tyr Gly Leu Tyr Ile Pro Ala Phe Leu Leu Glu Leu Glu Phe
65 70 75 80

Ser Lys Tyr Glu Ala Lys Arg Ala Tyr Val Thr Ser Pro Gln Pro Trp
85 90 95

Ala Leu Ser His Gly Thr Ser Leu Ala Gly Ser Val Ser His Val Leu
100 105 110

Ser Gln Phe Leu Ala Glu Arg Ile Lys His Ile Leu Cys Asn Phe Thr
115 120 125

Gly Lys Arg Ile Leu Glu Ala Val Pro Gly Phe Phe Arg Leu Phe Leu
130 135 140

Met His Leu Phe Leu Leu Leu Ile Met Leu Arg Tyr Pro Ser Val Asn
145 150 155 160

Lys Ser Leu Ile Gln Leu Tyr Ala Lys Ser Tyr Glu Ser Gln Asn Arg
165 170 175

Gly Ile Ile Leu Gly Arg Pro Asp Thr Thr Lys Ile Asn Leu Lys Leu

180 185 190

Asn Ser Ser Pro Thr Ser Leu Ser Pro
195 200

<210> 268
<211> 321
<212> PRT
<213> Homo sapiens

<400> 268

Met Asn Gln Thr Leu Asn Ser Ser Gly Thr Val Glu Ser Ala Leu Asn
1 5 10 15

Tyr Ser Arg Gly Ser Thr Val His Thr Ala Tyr Leu Val Leu Ser Ser
20 25 30

Leu Ala Met Phe Thr Cys Leu Cys Gly Met Ala Gly Asn Ser Met Val
35 40 45

Ile Trp Leu Leu Gly Phe Arg Met His Arg Asn Pro Phe Cys Ile Tyr
50 55 60

Ile Leu Asn Leu Ala Ala Ala Asp Leu Leu Phe Leu Phe Ser Met Ala
65 70 75 80

Ser Thr Leu Ser Leu Glu Thr Gln Pro Leu Val Asn Thr Thr Asp Lys
85 90 95

Val His Glu Leu Met Lys Arg Leu Met Tyr Phe Ala Tyr Thr Val Gly
100 105 110

Leu Ser Leu Leu Thr Ala Ile Ser Thr Gln Arg Cys Leu Ser Val Leu
115 120 125

Phe Pro Ile Trp Phe Lys Cys His Arg Pro Arg His Leu Ser Ala Trp
130 135 140

Val Cys Gly Leu Leu Trp Thr Leu Cys Leu Leu Met Asn Gly Leu Thr
145 150 155 160

Ser Ser Phe Cys Ser Lys Phe Leu Lys Phe Asn Glu Asp Arg Cys Phe
165 170 175

Arg Val Asp Met Val Gln Ala Ala Leu Ile Met Gly Val Leu Thr Pro
180 185 190

Val Met Thr Leu Ser Ser Leu Thr Leu Phe Val Trp Val Arg Arg Ser
195 200 205

Ser Gln Gln Trp Arg Arg Gln Pro Thr Arg Leu Phe Val Val Val Leu
210 215 220

Ala Ser Val Leu Val Phe Leu Ile Cys Ser Leu Pro Leu Ser Ile Tyr
225 230 235 240

Trp Phe Val Leu Tyr Trp Leu Ser Leu Pro Pro Glu Met Gln Val Leu
245 250 255

Cys Phe Ser Leu Ser Arg Leu Ser Ser Ser Val Ser Ser Ser Ala Asn
260 265 270

Pro Val Ile Tyr Phe Leu Val Gly Ser Arg Arg Ser His Arg Leu Pro
275 280 285

Thr Arg Ser Leu Gly Thr Val Leu Gln Gln Ala Leu Arg Glu Glu Pro
290 295 300

Glu Leu Glu Gly Gly Glu Thr Pro Thr Val Gly Thr Asn Glu Met Gly
305 310 315 320

Ala

<210> 269
<211> 9
<212> PRT
<213> Artificial

<220>
<223> Novel Sequence

<400> 269

Ala Pro Arg Thr Pro Gly Gly Arg Arg
1 5

<210> 270
<211> 20
<212> DNA
<213> Artificial

<220>
<223> Novel Sequence

<400> 270
ctgtctctct gtcctcctcc 20

<210> 271
<211> 22
<212> DNA
<213> Artificial

<220>
<223> Novel Sequence

<400> 271
gcaccgatct tcattgaatt tc 22

<210> 272
<211> 33
<212> DNA
<213> Artificial

<220>
<223> Novel Sequence

<400> 272
gatcaagctt ggatgaacca gactttgaat agc 33

<210> 273
<211> 31
<212> DNA
<213> Artificial

<220>

<223> Novel Sequence

<400> 273
gatcctcgag ctcaagcccc catctcattg g 31